eISSN (Online): 2598-0580

Bioscientia Medicina: Journal of Biomedicine & Translational Research

Journal Homepage: www.bioscmed.com

Does Electroencephalography Result Affect the Success of Treatment for Epilepsy Patients?

Sri Handayani[1,2], Yunni Diansari[1], Selly Marisdina[1], Nova Lestari [3], Sri Yani[3]

[1]Lecturer in Neurology, Faculty of Medicine, Universitas Sriwijaya, Palembang
[2]Student of Biomedical Program, Faculty of Medicine, Universitas Sriwijaya, Palembang
[3]Residents of Neurology, Faculty of Medicine, Universitas Sriwijaya, Palembang

ARTICLE INFO

Keywords:
Electroencephalography
Treatment success

Corresponding author:
Sri Handayani

E-mail address:
srihandayani@fk.unsri.ac.id

All authors have reviewed and approved the final version of the manuscript.

https://doi.org/10.32539/bsm.v5i2.205

ABSTRACT

Background: Approximately there is 50 million people with epilepsy in the world. Currently, pharmacological management is the most therapeutic option. However, about 30% of patients will develop drug-resistant epilepsy. Many factors are thought to affect the treatment success. This study was conducted to determine the relationship between electroencephalographic results and epilepsy treatment success. **Methods:** This is cross sectional observational study. Inclusion criteria was epileptic patients aged > 18 years and had received epilepsy treatment for at least 1 year. The chi-square test is performed to see the relationship between research variables. **Results:** EEG results has an effect on the success of therapy (p 0.027). The most common type of epileptiform abnormality is sharp waves. The most epileptiform amplitude and location were 80 microvolts and in the temporal lobe. **Conclusion:** There is a significant relationship between EEG abnormalities and the epilepsy treatment success.

1. Introduction

According to the *World Health Organization* (WHO) there are about 50 million people with epilepsy in the world and the active epilepsy population between 4 and 10 per 1000 population per year. The prevalence of epilepsy in developing countries is higher than in developed countries, which is around 5-74 per 1000 people. The Epilepsy Study Group of the Indonesian Neuroslogist Association (Pokdi Epilepsi PERDOSSI) conducted a study at 18 hospitals in 15 cities in 2013 for 6 months, of which there were 2288 patients consisting of 487 new cases and 1801 old cases.[1]

Currently, pharmacological management is still a widely used therapeutic option.[2] This epilepsy treatment aims to achieve a seizure-free state without drug side effects and optimal quality of life for people with epilepsy. However, about 30% of patients will experience drug-resistant epilepsy and will still experience a seizure even though they have used polytherapy with optimal doses.[3]

The cause of drug-resistant epilepsy is not certain. There are so many developing hypotheses. Several factors have been considered to determine the success of epilepsy treatment. One of the factors that are considered influencing the incidence of drug resistant epilepsy is the EEG result.

Research on the relationship between EEG on the success of epilepsy treatment has been widely carried out but has different and contradictory results. This study was to determine the relationship between EEG result and the success of treatment in epilepsy patients

who were treated at the neurology polyclinic, dr. Mohammad Hoesin Hospital Palembang. From the results of this study, it is hoped that it can become a consideration for immediate special management to prevent drug-resistant epilepsy.

2. Methods

This research is an analytic observational study with a cross sectional approach using primary and secondary data. The research was conducted at the neurology polyclinic of dr. Mohammad Hoesin (RSMH) Hospital Palembang from April 2020 to November 2020. The population was all epilepsy patients who were treated at the neurology polyclinic, dr. Mohammad Hoesin Hospital Palembang. Samples were all epilepsy patients who met the study criteria and the minimum sample size was 68. Sampling was carried out by consecutive methods. Inclusion criteria were patients aged 18 years or over, diagnosed with epilepsy and had received epilepsy treatment either monotherapy or polytherapy for at least 1 year and were still on medication at the time of sampling.

The dependent variable in this study was the successful treatment of epilepsy patients who were treated at the Neurology polyclinic Dr. Mohammad Hoesin Palembang, while the independent variable is the EEG description. Operational limitation of the success of therapy in this study is the response to treatment, namely control of seizures in the last 1 year after receiving OAE with adequate therapeutic doses. If a wake-up-free state is achieved after using OAE, the treatment is said to be successful. If an awakening-free state is not achieved then treatment is not successful.

The study began with data collection of epilepsy patients from primary data at the neurological polyclinic, secondary data from medical records, then recording patients who entered the study criteria. Data collection was carried out using the form provided and for primary data accompanied by an informed consent form. Furthermore, the research subjects were recorded including general characteristics namely patient name, age, gender, education, frequency of seizures, history of epilepticus status, type of seizure, waiting time to start treatment, initial response to treatment, type of treatment and EEG picture. Data were analyzed using the *SPSS 22* for Windows program which consists of univariate analysis used to describe the characteristics of the sample by presenting the frequency distribution of each variable studied. Bivariate analysis using *Chi-square* test 95% CI $p < 0.05$ to determine the relationship between EEG image patterns and treatment success. And finally the data from the results of this study are presented in the form of tables and informative narratives.

This study has received certificate of Ethical Approval from the Ethic Committee of Mohammad Hoesin Hospital Palembang (No.93/kepkrsmh/2020).

3. Result

There were 68 patients that met the research criteria in this study. The characteristics of the research subjects can be seen in table 1. The results showed that more than half of the study subjects were over 40 years old and the most had onset of epilepsy when they were ≥ 15 years old (85.3%). The women subjects is more than men which can be found in 39 people. Meanwhile, based on the latest education status, the most patients were with high school education.

Epilepsy with symptomatic etiology was greater than idiopathic epilepsy. Most patients experienced seizure episodes less frequently (<1 time / month) where it was seen in 40 patients and the general seizure dominates in this study and is found in 83.8%. The majority of patients did not experience status epilepticus. There were more people with waiting time to start treatment ≤ 5 months (88.2%). In measuring the initial response to treatment, there were more patients who responded well, namely 49 people (72.1%). The most common type of treatment was anti-convulsant monotherapy. The success of therapy as assessed by controlled epilepsy symptoms in patients was found in 48 people (70, 6%). EEG results were most commonly found in the form of epileptiform.

In this study, bivariate analysis was conducted to determine the significance of the relationship between

the two variables. In this case, the relationship between the independent variable and the EEG description was analyzed using the Chi-square test analysis of 95% CI p <0.05, which requires that the expected count in each cell should not be less than 5. If this requirement is not met, then The Fischer Exact Test analysis can be used as an alternative.

The results of the analysis of the EEG result showed that the abnormality of the EEG had a significant effect on the success of therapy with a value of p = 0.027. The group of patients with normal EEG results had a therapeutic success of 68.8% while the group of patients with abnormal EEG results had a therapeutic success of 31.2%. The types of abnormalities found can be seen in table 3, namely the most epileptiforms epileptiform types were sharp waves (table 4). The most common epileptiform amplitude is 80 microvolts with the common location being the temporal lobe.

Table 1. Characteristics of Research Subjects

	Epilepsy	
	Frequency (n)	Percentage (%)
Age		
- <20 year	7	10.3
- 21-39 years	25	36.8
- ≥ 40 year	36	52.9
Age of onset		
- <15 year	10	14.7
- ≥ 15 year	58	85.3
Gender		
- Male	29	42.6
- Women	39	57.4
Educational status		
- SD	0	0.0
- Junior High	8	11.8
- High school	52	76.4
- PT	8	11.8
Etiology		
- Idiopathic	32	47.1
- Symptomatic	36	52.9
Seizures Frequency		
- Rarely	40	58.8
- Often	28	41.2
Type of seizure		
- Focal	11	16.2
- General	57	83.8
Status Epilepticus		
- Not there is	58	85.3
- There is	10	14.7
Long waiting time to start treatment		
- < 5 months	60	88.2
- > 5 month	8	11.8
Initial response to treatment		
- Response	49	72.1
- No response	19	27.9
Type of Treatment		
- Monotherapy	40	58.8
- Polytherapy	28	41.2
Therapeutic Success		
- Success	48	70.6
- Unsuccessful	20	29.4

EEG Features		
- Epileptiform and Slowing	15	22.1
- Epileptiform	24	35.3
- Slowing	13	19.1
- Normal	16	23.5

Table 2. Relationship between EEG abnormalities and the success of therapy

		Therapeutic success	
		Success	Unsuccessful
EEG Abnormalities	Abnormal	33 (68.8)	19 (95)
	Normal	15 (31.2)	1 (5)

Fisher's Exact Test, p = 0.027

Table 3. Relationship between type of EEG abnormality and treatment success

		Therapeutic success	
		Success	Unsuccessful
Types of EEG Abnormality	Epileptiform with slowing	7 (21.2)	8 (42.1)
	Epileptiform	17 (51.5)	7 (36.8)
	Slowing	9 (27.3)	4 (21.1)

Likelihood ratio p = 0.284

Table 4. Types of Epileptiform

		Therapeutic success	
		Succeess N (%)	Unsuccessful
Types of epileptiform activity	Spike	5 (20.8)	1 (6,7)
	Sharp	15 (62.5)	8 (53.3)
	Polispike	1 (12.5)	4 (26.7)
	Spike wave complex	3 (12.5)	2 (13.3)

4. Discussion

In this study, it was found that the age range was 20-67 years with the largest age being ≥ 40 years when this study began. Patients were found to have a greater age of onset ≥ 15 years, which is 85.3%. This is probably because the patients who come to the neurology polyclinic are adults (≥ 18 years old), while for cases of pediatric epilepsy going to the pediatric polyclinic. Kotsopoulos IAW et al study in 2002 explained that the incidence of epilepsy over time seems to decrease in children, while it increases in the elderly.[4] Epilepsy patients aged ≥ 20 years are usually caused by head trauma, brain tumors, vascular disorders, metabolic disorders and Alzheimer's. [5]

Women sample were more than 57.4%. This is in accordance with the research conducted by Handayani S in 2019 which stated that women with epilepsy were 51.6% more and male 48.4%. The CDC Epilepsy Research Program in 2005 also showed that women with epilepsy were 55.9%. This phenomenon is thought to be related to hormonal status in women. This can be explained that everyone has a brain with their respective threshold of awakening whether they are more resistant or less resistant to seizures.[2] In theory, seizures do not occur randomly. Seizures tend to cluster in the majority of men and women with epilepsy. Seizure clusters often show periodicity. When the periodicity of seizure exacerbations coincides with the menstrual cycle, it is called catamenial epilepsy.[6]

The educational level of epilepsy patients is mostly at the secondary education level and above, namely

88.2% with most of them have high school education at 76.4%. This is accordance with the research of Mohammadi N et al in Iran that most of the epilepsy patients are also educated from middle to high school, namely 41.8% have high school education and 20.3% have tertiary education.[7] In the research of Hussein MJ in Jordan shows that most of the epilepsy patients have middle to lower education, namely 52.5%. The large number of epilepsy sufferers are middle and lower education because this study has 49.5% of research subjects who are still school students starting from the age of 14 years. Education level is a demographic characteristic that can influence timing of initiation of treatment and clinical outcomes.[8]

Based on the results of this study, the etiology of epilepsy patients who went to the outpatient clinic of RSMH was mostly symptomatic epilepsy. This is in accordance with Handayani S's research which stated that 62.6% of symptomatic epilepsy was found and also in accordance with the data presented in the study of Tedrus et al which stated that 67.2% of cases of symptomatic epilepsy were found.[9] The cause is not clearly found, it is possible that in some cases there is a genetic relationship or genetic predisposition.[10,11] Idiopathic epilepsy is more common in people with epilepsy at a young age. In symptomatic epilepsy, Factors causing epilepsy seizures can be identified due to structural abnormalities or lesions in the brain such as head trauma, meningitis, encephalitis, cerebrovascular disease, brain tumors or labor injuries that result in anoxia in infants. Symptomatic epilepsy can appear at the time of brain damage or later in life.[2,12] Patients with symptomatic epilepsy etiology were more frequently found in this study in accordance with the greatest age prevalence found in this study, at ≥ 40 years old. This is synergistic with Guo Y et al study in China showing that stroke is the most common cause of epilepsy in elderly individuals (48.7%), and this finding is comparable with other reports in the medical literature describing the Chinese population and non-Chinese. In the study, all patients were categorized by place of residence and age. The study showed that more than half of epilepsy cases in the urban group or older were associated with stroke.[13] Cortical lesions and stroke severity are independent predictors of post-stroke epilepsy.[14] Therefore, urgent steps should be taken to reduce stroke rates, early preventive measures and lifestyle modifications to moderate risk factors for epilepsy.

In this study, most of the epilepsy seizures were general seizures, namely 83.8%. In Sirait study, there were also similar results that the highest proportion of epilepsy patients based on seizure classification was general epilepsy (79.4%).[15] In Conrad J study, the highest proportion of epilepsy sufferers based on the characteristics of the seizure was generalized 57.1%, simple focal generation was 22.5% and complex focal was 16.3%.[16] It was according to the widely adopted classification was first proposed by Gastaut in 1970 and then revised repeatedly by the Commission on Classification and Terminology of the International *League Against Epilepsy* (ILAE) 1981. This classification divides the seizure into two, focal or partial and general seizures. Partial seizures are confined to certain areas of the cerebral cortex, only certain parts of the body are usually involved, at least initially. In contrast, generalized seizures appear to be diffuse areas of the brain. Generalized seizures arise from both hemispheres of the brain simultaneously. [17]

Most of the epilepsy sufferers experienced initial seizure frequency <1 time a month was 58.8% while the seizure more than one time a month was 41.2%. In the data presented in the CDC Epilepsy Program study in 2005 which states that 55.1% reported no seizure in the last 3 months, 15.3% reported one seizure, and 28.6% reported more than one seizure.[18] Initial seizure frequency pre-treatment level is a predictor of drug-resistant epilepsy which has been proven through several studies. In a study on experimental animals with temporal lobe epilepsy, found resistance to phenobarbital in all experimental animals with a high frequency of seizures before treatment. Previous research stated that in the non-respondent group of phenobarbital the majority showed hippocampal damage.[19,20]

In this study, it was found that the majority of

patients did not experience status epilepticus as much as 85.3%. This was possible because the population in this study also had more epilepsy patients who were adherent to taking medication so that the incidence of status epilepticus was less.

Most of the patients in this study were found to experience a long waiting time for initiation of the treatment. The less or equal to 5 months group was 88.2% and more than 5 months group was 11, 8%. This is possible because the population in this study also had more epilepsy patients who had high school education so the decision to begin the treatment could be made more quickly. In the study of Sinha A et al, it was also found that most of the length of waiting time to start treatment was less than 3 months was 83.5%, 4-6 months 5.1%, 2 months 1.9%, 10-12 months 5.1% and more than 12 months 4.4%.[21]

In this study, it was found that epileptic patients received more antiepileptic drugs with monotherapy with a proportion of 52.5% phenytoin, 30% valproic acid, 15% carbamazepine and 2.5% lamotrigine. Phenytoin is more widely used for antiepileptic monotherapy than other antiepileptic drugs. 41.2% of patients who received antiepileptic polytherapy was in accordance with Ranjana study that most of the patients received monotherapy antiepileptic drugs by 53.21% while polytherapy was 46.78% .[22] Tendean P. G et al study showed patients who received monotherapy antiepileptic drugs were 91.5% and 48.9% of patients were given phenytoin therapy.[23] The principle of epilepsy treatment is to start with one drug since most epilepsy responds to OAE monotherapy. The choice of drug must be in accordance with the type of seizure and epilepsy. The principle of epilepsy management is to achieve seizure-free without experiencing adverse drug reactions, so ideally in the form of monotherapy with the lowest dose of drugs that can control seizures.[24] According to the PERDOSSI Epilepsy Management Guidelines, phenytoin and carbamazepine are effective drugs used as monotherapy in focal, secondary generalized seizures. , and tonic clonic, this could explain why phenytoin was found to be the most used in epileptic patients.

According to EEG result patients, 76.5% had abnormal EEG and the normal EEG were 23.5%. Patients who showed abnormal EEG had epileptiforms were 35.3%, 19.1% slowing with epileptiform and 22.1% slowing. This is similar to Handayani study showed that from the results of the EEG examination, 56.3% had abnormal EEG. The same thing was also found in Tendean P. G et al study that patients who had an EEG examination, 60% showed abnormal EEG, while 40% of patients showed normal EEG results.[23] Electroencephalography is a recording of the brain's electrical activity by placing leads on the scalp, or directly to the surface of the brain during surgery. Interictal EEG recording was performed to look for epileptiform waves that showed the inhibitory postsynaptic excitation process associated with hypersynchronous neuronal firing. Other abnormalities such as focal or general slow waves may be seen in patients with epilepsy but are not specific for epilepsy. Transient focal slowing may reflect inhibition caused by undetected deep interictal spikes or pathological changes such as nerve loss and gliosis, which are common in chronic epilepsy. However, focal slowing is present in many conditions other than epilepsy, such as gliosis, stroke, and tumors.[23] On an EEG examination, 30-50% of cases can find no abnormality if only examined once. Repeated EEG examinations will increase the findings of changes in the electrical activity of the brain. [25]

On In this study, it was found that the EEG results had an effect on the success of therapy with p value = 0.027 ($\alpha < 0.05$). Research by Yilmaz et al stated that EEG abnormalities are a predictor of drug-resistant epilepsy. They said that both focal and multifocal spikes were the most common abnormality in both drug-resistant and non-drug resistant groups, but this disorder was significantly more frequent in the group with drug-resistant epilepsy.[25] In this study, the types of abnormalities found can be seen in **table 3.** The most epileptiforms with the types were sharp waves **(table 4).** The most common epileptiform amplitude is 80 microvolts with the common location being the temporal lobe.

5. Conclusion

There is a significant relationship between EEG image abnormalities and the success of epilepsy treatment. Further research is needed to specifically assess the epileptiform characteristics of the EEG results both in ictal or interictal EEG.

6. Conflict of interest

The authors declare were no conflict of interest.

7. Funding statement

The research and publication of this article were funded by DIPA of Public Service Agency of Universitas Sriwijaya 2020 (Reference number: SP DIPA-023/2020)

8. Author contribution

SH YN, SM design of study. YN, SM statistical analysis. NL, SY technical support. NL, SY administrative support. SH laboratory analysis. SH YN drafted the manuscript. SH revised manuscript.

9. References

1. Kusumastuti K, Gunadharma S, Kustiowati E, Guidelines for the Management of Epilepsy. Airlangga University Press, 2014
2. Harsono, Kustiowati E, Gunadharma S. Guidelines for the management of epilepsy. 4th ed. Jakarta. PERDOSSI, 2012:3-19
3. Kwan P. Brodie MJ. Early identification of refractory epilepsy. N Eng J Med. 2000; 342 (5): 314-319
4. Kotsopoulos IAW, Van Merode T, Kessels FGH, De Krom MCTFM, Knottnerus JA. Systematic review and meta-analysis of incidence studies of epilepsy and unprovoked seizures. Epilepsia 2002; 43 (11): 1402-1409. doi: 10.1046 / j.1528-1157.2002.t01-1-26901.x
5. Sirait E, Lubis R, Hiswani. Characteristics of Hospitalized Epilepsy Patients at Haji Adam Malik Hospital Medan. Resipotori USU 2014.
6. Herzog AG. Catamenial epilepsy: Definition, prevalence of pathophysiology and treatment. Elsevier 2008; 17: 151-159. https://doi.org/10.1016/j.seizure.2007.11.014.
7. Mohammadi N, Kian S, Davoudi,F, Nia SMAA, Nojomi M. Psychometric evaluation of the Persian version of the quality of life in epilepsy inventory-31. Iranian Journal of Neurology 2013; 144-8.
8. Hussein MJ, El-Qaderi S. Socio-demographic characteristics of adolescents with epilepsy in Northern Jordan. Elsevier 2002; 483-8. https://doi.org/10.1016/S1059-1311(02)00133-4,
9. Tedrus GMAS, Fonseca LC, Nogueira JE, Pazetto D. Epilepsy with onset at over 50 years of age: clinical and electroencephalographic characteristics. Scielo 2011;780-5. http://dx.doi.org/10.1590/S0004-282X2012001000006.
10. Johnson MR, Sander JW. The clinical impact of epilepsy genetics. J. Neurol. Neurosurg. Psychiatry 2001; 70 (4):428–430. https://doi.org/10.1136/jnnp.70.4.428.
11. Gourfinkel-An I. [Genetic aspects of epilepsy]. EMC Neurologie 2009; 160 (17):1–14.
12. Beghi E, Giussani G, Abd-Allah F, Abdela J, Abdelalim A, Abraha HN, et al. Global, regional, and national burden of epilepsy, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol. 2019; 18 (4):357–75. https://doi.org/10.1016/S1474-4422(18)30454-X
13. Guo Y , Yu L , He B , Li S , Zhu O, Sun H. Aetiological Features of Elderly Patients with Newly Diagnosed Symptomatic Epilepsy in Western China. BioMed Research International. 2018. https://doi.org/10.1155/2018/4104691.

14. T. Tanaka and M. Ihara, “Post-stroke epilepsy,” Neurochemistry International 2017; 107:219–228. https://doi.org/10.1016/j.neuint.2017.02.002.
15. Loscher W, Schmidt D. Drug resistance in epilepsy: Putative neurobiologic and clinical mechanism. Critical Review; Epilepsia. 2005; 46 (6): 858-877. https://doi.org/10.1111/j.1528-1167.2005.54904.x.
16. Conrad J, Pawlowski M, Dogan M, Kovac S, Ritter MA, Evers S. Seizures after cerebrovascular events: Risk factors and clinical features. Elsevier 2013:275–288. https://doi.org/10.1016/j.seizure.2013.01.014
17. Goldenberg MM. Overview of Drugs Used For Epilepsy and Seizures: Etiology, Diagnosis, and Treatment. 2010; 35 (7):392–415.
18. Kobau R, Zahran H, Thurman DJ, Zack MM, Henry TR, Schachter SC, Price,PH. Epilepsy Surveillance Among Adults - 19 States, Behavioral Risk Factor Surveillance System, 2005. MMWR. 2008; 57:1-20.
19. Loscher W, Brandt C. High seizure frequency prior to antiepileptic treatment is a predictor of pharmacoresistant epilepsy in a rat model of temporal lobe epilepsy. Epilepsia 2010; 51 (1): 89-97. https//doi.org/10.1111/j.1528-1167.2009.02183.x
20. Loscher W. Current knowledge on basic mechanisms of drug resistance. In Kahane P, Berg A, Loscher W, Nordli D, Perucca E, eds. Drug- Resistant Epilepsies. United Kingdom. John Libbey Eurotext 2008:47- 57.
21. Sinha A, Mallik S, Sanya D, Sengupta P, Dasgupta S. Healthcare-seeking behavior of patients with epileptic seizure disorders attending a tertiary care hospital, Kolkata. Indian Journal of Community Medicine, pp. 25-9, 2012. https://dx.doi.org/10.4103%2F0970-0218.94018.
22. Triono A. Prognostic Factors for Failure of Epilepsy Therapy in Children on Monotherapy. Sari Pediatrics. 2014; 16 (4): 248-53.
23. Ranjana G, Dwajani S, Kulkarni C, Sarma GRK. The sociodemographic, clinical and pharmacotherapy characteristics influencing quality of life in patients with epilepsy: A cross-sectional study. J Neurosci Rural Pract. 201; 5 :7–12. https://dx.doi.org/10.4103%2F0976-3147.145193
24. Tendean PG, Karema W, Mawuntu A. The description of people with epilepsy based on ILAE 1989 at the Neurology Polyclinic, Prof. Dr. RD Kandou Manado. Journal E-Clinic 2016; 4(1).
25. Trescher WH, Lesser RP. The Epilepsies. In: Bradley WG, Daroff RB, Fenichel GM, Jankovic J, eds. Neurology in Clinical Practices. Elsevier Health Science. 5th ed. 2007:1909–46.