Level Of Compliance With The Use Of Anti-Epileptic Medication In Outpatient Patients At RS X Jepara

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Abstract. Epilepsy is a recurrent paroxysmal seizure attack without provocation, with an interval of more than 24 hours. The most common symptom of epilepsy is seizures. Compliance with taking medication in epilepsy patients is one of the important factors for the success of therapy. The purpose of this study was to determine the level of compliance with the use of anti-epileptic drugs at X Hospital Jepara. This study is a descriptive observational study with quantitative data types. Data collection was carried out prospectively in April-May 2023 by observing some objects. The subjects in this study were 70 respondents, and data collection used the MMAS-8 questionnaire. The results of the questionnaire score have 3 categories: high compliance score 8, moderate compliance 6-7, and low compliance <6. Based on this study, it shows that people with epilepsy based on male gender were 39 respondents (55.7%) more than women. Based on age characteristics, the largest number was found in the adult group (26-45 years) at 32 respondents (45.7%). Based on the highest level of education, 32 respondents (45.7%) were at the high school level, while based on occupation, the most were housewives, 23 respondents (32.9%). Based on the profile of drug use, there are 2 therapies, namely a combination of 2 drugs (polytherapy) and monotherapy. The most common use of polytherapy is Valproic acid and Phenytoin, 43 respondents (61.43%), while the most frequently used monotherapy is Phenytoin, 17 respondents (24.29%). Based on the level of compliance, it is relatively low, namely 45 respondents (64.3%). Judging from the characteristics based on age, most are adults (26-45 years), based on gender, the most are male, the highest level of education is high school, and based on occupation, the most are housewives. Based on the profile of the use of polytherapy drugs, the most frequently used are Valproic acid and Phenytoin, while the most frequent monotherapy drug is phenytoin. The level of compliance with the use of outpatient epilepsy medication at X Hospital Jepara is relatively low.

Key words: Compliance, Antiepileptic Drugs, Outpatient

INTRODUCTION

Epilepsy is defined as recurrent unprovoked paroxysmal seizures at intervals of more than 24 hours without an apparent cause. (Ministry of Health of the Republic of Indonesia, 2017). In 2022, it was shown that there were 50 million epilepsy sufferers worldwide, with 80% of sufferers in developing countries (WHO, 2022). Epilepsy is a condition of unprovoked seizures, while status epilepticus is seizure activity that does not improve spontaneously or repeated seizures without any improvement between seizures.(Ernawati and Islamiyah, 2019)The most common symptom of epilepsy is a seizure. A seizure can be defined as a clinical symptom caused by abnormal, excessive, and unbalanced neuronal activity in the brain.

Epilepsy is a significant population disorder worldwide, affecting approximately 50 million people. The estimated proportion of the general population with active seizures (continuing seizures or requiring treatment) at any given time is between 4 and 10 per 1,000 people (WHO, 2022). Forty percent of children with epilepsy experience status epilepticus before the age of 2 years, and 75% of children with epilepsy experience status epilepticus as the first symptom of epilepsy (Ministry of Health of the Republic of Indonesia, 2017). Current antiepileptic drugs can be divided into several categories based on their mechanism of action, namely, sodium channel blockers, GABA action enhancers, calcium channel inhibitors, glutamate blockers, and drugs with other mechanisms that are not yet known (Ikawati and Anurogo, 2018).

The challenge that prevents therapy with AED (Anti-Epileptic Drug) not to being achieved is adherence or compliance. (Widyati et al., 2013). Medication adherence is a person's behavior in taking medication according to the prescribed dosage and time within a specific timeframe. Most epilepsy patients require long-term therapy (>3 months); the longer the therapy, the greater the chance of non-adherence. Various factors reduce medication adherence in epilepsy patients. These factors vary depending on the sociodemographic conditions of a region (Mawuntu *et al*., 2019).

Non-adherence to treatment can lead to increased duration of illness, worsening medical

conditions, lengthened hospital stays, or even death. Non-adherence to epilepsy treatment increases the risk of recurrent seizures and increases the risk of refractory epilepsy by 10-20% (Kardas, Lawek and Matyjaszczyk, 2013). Permana and Hadi's 2021 study showed that 13.3% of patients were compliant, 23.3% were moderately compliant, and 56.7% were non-compliant. Other studies have shown that non-compliance was due to forgetting doses (47.5%) and lack of time to take AEDs (39.2%) (Ernawati and Islamiyah, 2019).

X Hospital Jepara serves as a referral center for epilepsy patients from the primary healthcare facilities in Jepara and its surrounding areas, with an average of 50 patients per month. Based on the above background, a study on the "Level of Compliance with Antiepileptic Drug Use at X Hospital Jepara" is needed.

This study used a descriptive observational method with a prospective approach. Data were obtained using SPSS with univariate analysis. Compared with previous studies, this study focuses more on the level of adherence in epilepsy patients using antiepileptic drugs, both monotherapy and polytherapy. The advantages of this study are the use of the MMAS-8 questionnaire by Morisky, which can identify barriers to non-adherence, is easy to score, and can be used for research on chronic diseases such as epilepsy (Culig and Leppée, 2014).

METHODS

This study uses descriptive observational research with quantitative data. Quantitative research involves maintaining distance between the researcher and the object of study, using formal, standardized, and measurable instruments. Data collection in this study was conducted prospectively. Data were collected prospectively by observing many subjects who were being studied to determine an event that had not yet occurred or had occurred. The population studied in this study was all outpatients diagnosed with epilepsy and visiting the Sultan Hadlirin Islamic Hospital in Jepara. The population in this study was 120 patients, while the sample used was 70 outpatients diagnosed with epilepsy who met the inclusion criteria. Respondent characteristics can be seen based on age, gender, occupation, and education level.

This study was conducted in April-May 2023. This study was conducted at X Hospital, Jepara Raya street, Jepara-Bangsri km. 03 Jepara, Central Java 59645. The data analysis taken in this study was data from neurology polyclinic patients at X Hospital Jepara who received prescriptions for epilepsy medication with the inclusion criteria. Data analysis was carried out using the SPSS (Statistical Program for Social Science) program, and data processing was carried out with univariate analysis. Univariate analysis was used to measure patient characteristics, including age, gender, type of medication, and level of compliance. Using the Frequency test (Ahyar *et al*., 2020).

RESULTS AND DISCUSSION

Respondent Characteristics

This study was conducted at the Neurology Clinic of X Hospital Jepara on 70 epilepsy patients who met the inclusion criteria. Data collection took place between April and May 2023. The study was approved by the Research Ethics Committee of Muhammadiyah University of Purwokerto under research number KEPK/UMP/78/III/2023.

Table 1. Characteristics of Epilepsy Patients at the Neurology Clinic X Hospital, Jepara

Patient Characteristics	Total (N) = 70	Percentage (%)
Age		
20-25 (Teenagers)	14	20
26-45 (Adult)	32	45.7
46- 65 (Elderly)	17	24.3
>65 (Seniors)	7	10
Gender		
Man	39	55.7
Woman	31	44.3
Education		
No school	2	2.9
Elementary School	8	11.4

Patient Characteristics	Total (N) = 70	Percentage (%)
Junior High School	21	30
Senior High School	32	45.7
College	7	10
Work		
Retired/Not Working	11	15.7
Private employees	8	11.4
Civil Servants/TNI/POLRI	6	8.6
Housewife	23	32.9
Self-employed/Trader	21	30

Source: Secondary data (2023)

a. Age

In this study, patient characteristics based on age showed that the most common age group was 26-45 years (adults) with 32 respondents (45.7%). This is likely due to conditions such as post-traumatic stress disorder, stroke, brain tumor, or other causes. Generally, fatigue, excessive thinking, and seizures are common in epilepsy sufferers. As research shows (Ponnusamy, 2017)who said that 2017Focal epilepsy often occurs in adults and can be caused by stroke, head trauma, post-operative vascular disorders, and Alzheimer's.

In other studies, it was shown that adults (18-65 years) consisted of 49 respondents (80.3%). The results of this study indicate that most epilepsy occurs in the adult age group, most likely due to the habit of people doing a lot of work during their productive years. (Anindya et al., 2021).

Different from research. (Ruspanah, 2018), The study stated that the majority of respondents were aged 17-25 years, with 21 respondents (50%). The results of this study indicate that adolescents with epilepsy have a greater cognitive capacity than children to understand and question the unpredictable and uncontrolled nature of seizures.

b. Gender

This study showed that there were more men than women, with 39 respondents (55.7%), while there were 31 women (44.3%). This is likely due to men experiencing head injuries more frequently than women.

Based on research (Saraswati *et al.*, 2022), the prevalence in Asian countries is 76 men (51%), while the prevalence in Asian countries is 73 women (49%). While the cause is unknown, this difference is thought to be due to the significant hormonal influence of epilepsy. The female sex hormones, estrogen and progesterone, influence the seizure threshold to some extent, making men more susceptible to epilepsy.

According to epilepsy studies (PERDOSSI, 2014), this explains that in Asian countries, the prevalence of epilepsy is higher in males than in females. Although the exact cause is unknown, it is thought to be due to hormones significantly influencing epilepsy.

c. Work

This study showed that, based on occupational characteristics, the majority of respondents were housewives, with 23 respondents (32.9%). This finding is due to the rural nature of the area and the prevalence of women marrying young and solely caring for their families.

Based on the research results, as many as 109 respondents (68.1%) said that people with epilepsy should not have the same job as people without epilepsy because they are not allowed to do heavy work or be in dangerous places such as near the sea or water, and drive motorized vehicles (84 people/52.5%) or are afraid that it will interfere with their work.(Suryawijaya, Sam and Gelgel, 2019).

d. Level of education

This study showed that the highest educational level for respondents, 32 (45.7%), was high school. This finding is due to the cognitive impairment of epilepsy sufferers, who are unable to think at a higher level. The majority of people in the Jepara area work as fishermen, so they believe that a high school education is already considered high.

This research is almost the same as the research (Fatmi *et al.*, 2022)**.** The distribution of samples based on the highest level of education was in the high school group, with 16 people (44.4%). This is due to the cognitive dysfunction experienced by epilepsy sufferers, so that most epilepsy sufferers are only able to pursue education up to the high school level.

In another study, 25 people (41.0%) had a senior high school education. This finding may be due to the cognitive impairment experienced by most epilepsy sufferers, which limits their

education to high school. It could also be due to social pressures that stigmatize people with epilepsy as incapable of attending school, leading to a lack of confidence in continuing to the next level of education, which requires more critical thinking (Anindya *et al*., 2021).

Characteristics of Drug Use Profile

In this study, the characteristics of the drug use profile in outpatient epilepsy patients at Sultan Hadlirin Jepara Hospital were grouped based on the number of drugs and their use, which can be seen in Table 2.

Table 2. Characteristics of Outpatient Epilepsy Medication Use at X Hospital Jepara April-May 2023

Drug Use	Types of Drugs	Number (N)	Percentage (%)
Single	Phenytoin	17	24.29
	Valproic Acid	8	11.43
Combination of 2 Drugs	Valproic Acid + Phenytoin	43	61.43
	Phenobarbital + Phenytoin	2	2.86
	Total	**70**	**100.00**

Source: Secondary data (2023)

In this study, epilepsy use was divided into two categories: monotherapy and a combination of two drugs (polytherapy). The most frequently used single drug was phenytoin, with 17 respondents (24.29%), and valproic acid, with 8 respondents (11.43%). The most frequently used combination of two drugs was valproic acid and phenytoin, with 43 respondents (61.43%). Phenytoin is given in a single dose because it is an anticonvulsant and is a first-line drug in the treatment of epilepsy, as it works by reducing excessive activity in the brain, thus reducing seizures (Tedyanto *et al*., 2020)

The advantages of monotherapy over combination therapy include clearer and easier clinical observation, avoidance of overtreatment, the absence of unwanted drug interactions, and the absence of specific side effects associated with combination therapy, such as an increased risk of teratogenicity. In addition to the number of AEDs administered, adherence to therapy is also considered to influence the quality of life in epilepsy patients. When monotherapy is deemed to be failing to control seizures, the addition of an antiepileptic drug or its substitution is the next step (Permatananda, Budi Apsari and Harkitasari, 2019).

AED polytherapy is the combination of two or more AEDs to increase the efficacy (freedom from seizures) and tolerability of treatment.(Khairani and Sejahtera, 2019). The requirements for rational polytherapy administration in epilepsy patients include a combination of AEDs, both of which must have the following drug profiles: have different drug mechanisms of action, can be combined in small doses to provide maximum drug effects, and have different side effects.

Phenytoin monotherapy was more common at 37.7%, while phenobarbital was used in combination with 10.1% of patients, and only 11.7% of patients used combination polytherapy. This study differs from the use of phenobarbital (PERDOSSI, 2014). Phenytoin is widely used in clinical practice as a treatment for generalized tonic-clonic seizures and is known to be involved in impairments in concentration, memory, and visuomotor function. Phenytoin is an antiepileptic drug with greater cognitive effects than carbamazepine and valproic acid. Phenytoin affects not only memory but also thinking speed and psychomotor skills (Sekarsari, 2020).

The underlying mechanism by which phenytoin causes impaired memory function remains unclear, but its long-term use can cause a significant decrease in serum folate levels (Sanjiwani, Sugianto and Kasih, 2019).

Besides phenytoin, another single therapy for epilepsy is valproic acid, one of the most effective antiepileptic drugs (AEDs). Valproic acid is the drug of choice for children and adults with epilepsy with generalized or focal seizures and is a consistent and safe IV option for status epilepticus (Romoli *et al*., 2019).

The mechanism of action of this drug is by increasing Yaminobutyric acid (GABA) and the neurotransmitter glutamate, and is the most effective antiepileptic drug in treating generalized seizures (Nanau and Neuman, 2013).

According to Sambono *et al.* (2020), the percentage of patients using combination therapy with phenytoin and valproic acid was only 23% of the 100% of epilepsy cases using combination therapy. The use of combination therapy with phenytoin and valproic acid can minimize the risk of seizures but

does not affect magnesium levels in epilepsy patients, and no drug-related problems were found.

The results of this study indicate that another type of monotherapy is valproic acid (27.2%), which is one of the antiepileptic drugs prescribed in Indonesia. Valproate is used as a first-line medication and has been proven effective in treating patients with generalized epilepsy. Based on clinical data on the incidence rate, valproate administration is effective in treating all types of epilepsy (Tatum, 2010).

The mechanism of the combination of phenytoin and valproic acid is that phenytoin metabolism is inhibited by the presence of valproic acid, thereby increasing phenytoin toxicity. Valproic acid and phenytoin are antiepileptic drugs commonly used as monotherapy. Phenytoin is believed to be more effective for focal-onset seizures, and valproic acid is more effective for generalized-onset tonic-clonic seizures (with or without other types of generalized seizures) (Lacy, Armstrong, and Goldman, 2010).

The combination of phenytoin and phenobarbital was used in 54% of patients. This is a common combination used in the treatment of(Wijayatri, 2012). The mechanism of action of these two drugs has a mutually supportive mechanism of action, namely phenytoin as a Na channel blocker, while phenobarbital is a Gamma-Aminobutyric Acid (GABA) enhancer (Lee and Dworetzky, 2010).

Another common polytherapy option is the use of phenobarbital and phenytoin. These two drugs have complementary mechanisms of action: phenytoin acts as a Na channel blocker, while phenobarbital acts as a GABA enhancer. Polytherapy is considered rational if the AEDs used in combination have different mechanisms (Suryoputri, 2021).

Level of Compliance with Medication Use

In this study, the level of drug use in patients using the MMAS-8 epilepsy questionnaire at RSI Sultan Hadlirin Jepara can be seen in Table 3.

Table 3. Level of Compliance with Outpatient Epilepsy Medication Use at X Hospital, April-May 2023

Compliance	Total (N) = 70	Percentage (%)
Tall	5	7.1
Currently	20	28.6
Low	45	64.3

Source: (Secondary Data, 2023)

Based on Table 3, the level of compliance was high at 5 respondents (7.1%), while at 20 respondents (28.6%) it was low at 45 respondents (64.3%). This study can be concluded that the level of compliance in taking epilepsy medication is low because of forgetting to take medication, deliberately not taking medication, and forgetting to bring medication when traveling, which causes patients to relapse quickly.

Different from research (Ernawati and Islamiyah, 2021), it is known that the low compliance rate is 12.5%, for medium or moderate compliance it is 65%, and high compliance is 22.5%. Patient non-compliance with treatment can be caused mostly by the factor of forgetting to take medication (not taking it). The responses showed that the majority of patients had experienced forgetting to take their medication while taking antiepileptic drugs. This is closely related to the nature or characteristics of epilepsy, a neurological disease that can affect a patient's cognitive abilities and memory. Epilepsy can cause memory impairments due to the epilepsy itself, as well as age at the time of the diagnosis.

Another study categorized patient compliance into two categories: compliant and non-compliant. Twenty-nine (30.2%) patients were compliant, while 67 (69.8%) were non-compliant. Therefore, the non-compliance rate is higher than the compliance rate. Non-compliance can be seen in medication dosage, method, timing, and duration of medication use that are not in accordance with the instructions (Alkandari & Putri, 2021).

Ibrahim's 2019 study stated that the statistical test results obtained a p-value of 0.001, indicating a relationship between medication adherence and seizure occurrence during at least one year of treatment in epilepsy patients. With an OR of 0.480, respondents who were non-compliant with their medication had a 48-fold greater risk of experiencing frequent seizures. (Ibrahim, 2019).

In the 2019 study by Ernawati and Islamiyah, looking at the relationship between the level of compliance with the use of antiepileptic drugs and the incidence of seizures in epilepsy patients, it was found that there was a relationship between low levels of patient compliance and an increased incidence of seizures ($r = -0.348$), with a p value <0.05 or significant.

In Cullig and Leppee's (2014) study, Morisky's MMAS-8 questionnaire was used because it has

advantages over other questionnaires, such as its ability to identify barriers to non-adherence, ease of scoring, and its potential for use in research on chronic diseases such as epilepsy. The MMAS-8 method is more accurate, less expensive, and more capable of providing information on attitudes and beliefs about medications than pill count methods. This method influences the accuracy and validity of the questionnaire because it depends on the respondent's ability to understand the questions and their willingness to disclose information.

CONCLUSION

Based on research conducted on 70 respondents regarding the level of compliance with the use of anti-epileptic drugs in outpatients at X Jepara, it can be concluded that:

1. The characteristics of epilepsy patients based on age are mostly adults aged 26-45 years, with 32 respondents (45.7%). Based on gender, the highest is male with 39 respondents (55.7%), based on the highest level of education, the highest is high school with 32 respondents (45.7%), while based on occupation, the highest are housewives with 23 respondents (32.9%).
2. Based on the level of compliance with the use of antiepileptic drugs at X Jepara for the period April-May 2023, the high compliance rate was 7.1%, the moderate rate was 28.6%, and the low compliance rate was 64.3%.

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