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A comparison study between single aspirin antiplatelet and single clopidogrel antiplatelet on average period of recurrent stroke dr. Sayidiman Magetan

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ABSTRACT

Stroke is a common neurological disease that rapidly develops clinical signs of focal and global neurological deficits, lasts 24 hours or more, and leads to death. The danger that threatens stroke sufferers is recurrent strokes which can be fatal and result in a worse quality of life than the first attack. This condition indicates that the effect of antiplatelet drugs is not strong, or called antiplatelet resistance. Antiplatelet is a blood thinner used by stroke sufferers to prevent blood clots and treat the narrowing blood vessels in the legs, namely in peripheral artery disease. This research aims to compare single aspirin antiplatelet and single clopidogrel antiplatelet on the average period of recurrent stroke. This observational research employed a cross-sectional approach by processing the medical record data of stroke patients from 2018 to 2020 at dr. Sayidiman Magetan Regional Public Hospital. The obtained data were then analyzed and concluded. The results show that the mean duration of recurrent stroke on aspirin antiplatelet use is 357.88. Meanwhile, the mean duration of recurrent stroke in the antiplatelet clopidogrel is 138,59 days. Moreover, there is a significant difference between the use of a single aspirin antiplatelet and single clopidogrel antiplatelet on the duration of recurrent stroke with a ρ-value of 0.000.

1. Introduction

In 2017 the World Health Organization (WHO) declared that stroke ranks the second noncommunicable disease that causes death. Meanwhile, the American Health Association reported in the 2017 Heart Disease and Stroke Statistics that an American suffers from a stroke every 40 seconds, and an American dies due to stroke every four minutes (Benjamin et al., 2017). Based on the doctor's diagnosis, the national prevalence of stroke in Indonesia was 10.9% in 2018. East Java Province has ranked the seventh position (12.4%) of 34 provinces in Indonesia (Riskesdas, 2018).

Stroke is a common neurological disease that causes clinical signs, develops very quickly in the form of a focal and global neurological deficit, lasts for 24 hours or more, and leads to death. A stroke occurs when a blood vessel in the brain is blocked or broken so that it does not get the blood supply that carries oxygen; the fatal result of strike is cell death or brain tissues (Smith et al., 2015).

The danger that threatens stroke patients is the recurrent stroke that results in fatality and a worse quality of life than the first attack. The incidence of cardiovascular disease can still recur in some patients although they have applied antiplatelet therapy. Such a condition occurs because the antiplatelet medicine is less responsive and has a less strong influence; it is called antiplatelet resistance. The average incidence of resistant antiplatelet in stroke patients or transient ischemic attack (TIA) is 3-85% in aspirin and 28-44% in clopidogrel (Rakhmawati et al., 2019).

Antiplatelet is one of the blood-thinner medicine administered to stroke patients to prevent blood clots and peripheral artery patients to treat vasoconstriction in the limbs, i.e. on diseases (Karuniawati et al., 2015). (Masruhim, 2016) has discovered that aspirin is the most widely used antiplatelet medicine in 35 cases (48.6%), and the antiplatelet therapy of aspirin can more significantly prevent cardiovascular incidence than the risk of bleeding. Another study by (Putra et al., 2016) has revealed a relationship between levels of antiplatelet aspirin medication compliance and the incidence of recurrent stroke. Patients with low medication compliance have a higher risk of recurrent stroke attacks than patients with high medication compliance (Masruhim, 2016; Putra et al., 2016).

Based on the description above, the researchers are interested in comparing periods of recurrent strokes of patients who are administered to single aspirin antiplatelet and single clopidogrel antiplatelet in dr. Sayidiman Regional Public Hospital, Magetan. This study is expected to provide the latest data and could lower the number of deaths due to stroke.

2. Materials and Methods

2.1. Research Design

This research employed an observational study with a cross-sectional approach. The data of this research were medical records of recurrent stroke patients in dr. Sayidiman Regional Public Hospital, Magetan. The research samples were recurrent stroke patients who were administered single and combined antiplatelets. The samples were selected using the non-probability sampling method and the purposive sampling technique. The selected samples had met the inclusion criterion: inpatients who received antiplatelet therapy for at least three months.

2.2. Research Site and Time

This research was conducted in dr. Sayidiman Regional Public Hospital, Magetan. Jl. Pahlawan No.2, Tambran, Magetan District, Magetan Regency, East Java from February to March 2021.

2.3. Research Materials

The material of this research was medical records of recurrent stroke patients who had been administered single antiplatelet medicines for at least three months.

2.4. Working Procedures

The data were collected by taking notes of medical records of recurrent stroke patients who were hospitalized and diagnosed with the disease after they had been applying the antiplatelet therapy for at least three months in dr. Sayidiman Regional Public Hospital Magetan from January 2017 to January 2020. The collected data included age, sex, blood pressure, frequency of antiplatelet drug administration, and the period of recurrent stroke incidence.

2.5. Data Analysis and Presentation

The collected data were processed and analyzed using the "Statistical Analysis SPPS version 20." Before the statistical analysis, the normality test had been conducted (Kolmogorov-Smirnoff) to determine the normality of the data and find out what the statistical test would be applied. If the data on the average period of recurrent strokes in patients taking a single antiplatelet of aspirin and clopidogrel had not been normally distributed, the Mann-Whitney U test would have been conducted. In contrast, if the data had been normally distributed, the independent t-test would have been conducted. To examine the difference between the use of aspirin antiplatelet and clopidogrel antiplatelet, this study employed the following formulas. The value of $p < 0.05$ is considered significantly different. Meanwhile, the value of $p > 0.05$ is not significantly different.

3. Results and Discussion

This study involved 100 patients who met the inclusion criteria to be the research subjects. 50 of them have received the Aspirin, and the other 50 received have Clopidogrel. The research subjects consist of 38 men (38%) and 62 women (62%). The age data show that 73 patients (73%) are > 60 years old, and 27 patients (27%) are 20-60 years old.

Table 1. Characteristics of patients

Characteristics	Total (n)	Percentage (%)
Gender		
Men	38	38
Women	62	62
Total	100	100
Age		
20-60 years old	27	27
> 60 years old	73	73
Total	100	100

Table 1 shows that 62% of the patients are women because they have an estrogen hormone system that helps the LDL catabolism and the hepatic HDL uptake. The LDL catabolism decreases because the estrogen hormone levels decrease; thus, atherosclerosis that could trigger complications, including stroke, increases (Juwita et al., 2018). Such a condition more commonly occurs in menopausal women (Juwita et al., 2018). (Juwita et al., 2018) have revealed a similar situation that in dr. M. Djamil Central General Hospital, Padang, of the 32 respondents, 21 of them are women.

The age distribution of this research refers to the 2020 categories of the World Health Organization (WHO): 0-1 years old, 2-10 years old, 11-19 years old, 20-60 years old, and > 60 years old. This research has obtained that 73% of the respondents are > 60 years old. The ischemic stroke frequently occurs in > 60 years old patients because the function of their body organs, blood flow to the brain, and the arterial elasticity that constricts and stiffens the blood vessels have decreased. These conditions can increase the risk of hypertension and atherosclerosis, which can lead to ischemic stroke (Anggraini & Masruhim, 2016). This condition is supported by (Juwita et al., 2018) who have revealed that of 32 patients, 21 of them are >65 years old.

Table 2. Average uses of antiplatelet

Antiplatelet	Average use (months)
Aspirin	8
Clopidogrel	5

Table 2 shows that the average use of aspirin antiplatelet from the initial use to the recurrent stroke is eight months, and the average use of clopidogrel antiplatelet is five months. The average period of the incidence of recurrent stroke in the use of antiplatelet is presented in Table 3.

Table 3. The average period of the incidence of recurrent stroke in the use of antiplatelet

Antiplatelet	Total (n)	Average (days)	Median (days)	Min (days)	Max (days)	95% Cl (days)
Aspirin	50	357.88	241	103	1,104	267.63-439.13
Clopidogrel	50	162	133	93	572	138.59-185.41
Total	100					

Table 3 shows that the average recurrent stroke period of patients who are administered aspirin is 357.88 days. The minimum period of recurrent stroke is 241 days, and the maximum period is 1,104 days. This study has also found that the average recurrent stroke period of the patients administered aspirin is between an interval of 267.63 and 439.13 days. The average recurrent stroke period of patients who are administered clopidogrel is 162 days. The minimum period of recurrent stroke is 93 days, and the maximum period is 572 days. This study has also found that the average recurrent stroke period of patients administered to clopidogrel is between an interval of 138.59 and 185.41 days.

Comparison between Single Aspirin Antiplatelet and Single Clopidogrel Antiplatelet on Average Period of Recurrent Stroke

Before conducting the comparison test, this study had conducted the normality test. The normality scores of the recurrent stroke period of the patients administered aspirin and clopidogrel are summarized in Table 4.

Table 4 shows that data on the incidence of recurrent stroke is not normally distributed. Therefore, the Mann-Whitney U test should be conducted. The Mann-Whitney test investigated the average

recurrent stroke period of patients who were administered aspirin antiplatelet and clopidogrel antiplatelet. The results of this test are presented in Table 5.

Table 4. Normality of recurrent stroke period of patients administered to aspirin and clopidogrel

Antiplatelet	The average period of recurrent stroke	Normality
Aspirin	357.88 days	0.000
Clopidogrel	162 days	

Table 5. Comparison of the use of single aspirin antiplatelet and single clopidogrel antiplatelet on the average recurrent stroke period by Mann-Whitney U test

Antiplatelet	The average period of recurrent stroke	*ρ*-value
Aspirin	357.88 days	0.000
Clopidogrel	162 days	

Table 5 shows that there is a different recurrent stroke period between the use of aspirin antiplatelet agents and clopidogrel antiplatelet agents because the ρ-value is 0.000 < 0.05. The average recurrent stroke period of patients administered aspirin antiplatelet is 357.88 days, and the average aspirin antiplatelet administration is eight months. Meanwhile, the average recurrent stroke period of patients administered clopidogrel antiplatelet is 162 days, and the average clopidogrel antiplatelet administration is five months. This study has revealed that aspirin inhibits stroke recurrence longer than clopidogrel because aspirin is an antiplatelet agent that inhibits the blood clot formation of stroke patients; as a result, stroke recurrence can be prevented. Moreover, aspirin will prevent blood platelets to thicken the blood, thus the risk of clots can be reduced. Clopidogrel is a blood thinner to prevent heart attack in people who are newly suffered from heart disease, https://hellosehat.com/saraf/stroke/penyakit-stroke/ stroke, or blood circulation diseases (vascular peripheral disease). Clopidogrel is also used along with aspirin to treat worsening shortness of breath due to a recent heart attack and angina and to prevent blood congestion after certain cardiac procedures, such as a stent or heart ring placement. A blood thinner medicine works by inhibiting the occurrence of blood clots (Pokdi Stroke PERDOSSI, 2011).

This study has found that some respondents are administered aspirin but have a shorter period of recurrent strokes than those who are administered clopidogrel, or vice versa. Such a condition is probably triggered by several factors, such as the patients' medication noncompliance that results in non-optimal effects of aspirin or the patients' hypersensitive conditions that are not suitable for aspirin. The condition becomes worse because the previous medicine has not been replaced by another one until the patients are discharged. As a result, the doctor still prescribes aspirin for them. Non-optimal effects of aspirin can also occur due to two reasons (Amalia & Muflihatin, 2017). The first is aspirin resistance, a condition when the effects of aspirin reduce or are not significant. The second is patients' allergy to aspirin and thus, another antiplatelet, such as clopidogrel, should be recommended for the long term to prevent blood clots that can result in a recurrent stroke.

Aspirin and clopidogrel are equal types of antiplatelet but have different working mechanisms. Aspirin works as a blood thinner because it inhibits A2 thromboxane in the form of a substance that triggers blood clots. Meanwhile, clopidogrel belongs to the ADP class, which prevents blood clotting by binding the P2Y12 receptor in blood platelets. The side effect of aspirin and clopidogrel is gastrointestinal bleeding, but clopidogrel causes lower bleeding than aspirin. Moreover, the combination of aspirin and clopidogrel more likely increases the risk of bleeding than the use of a single antiplatelet. Antiplatelet therapy has more significant benefits for patients with the risk of high occlusive vascular.

However, according to (Masruhim, 2016), antiplatelet therapy brings a much greater risk of bleeding. Therefore, it is necessary to consider patients' conditions when selecting antiplatelet agents to prevent the incidence of recurrent stroke in a short time. Patients with speech disorders, weak limbs, and headaches in recurrent stroke should be initially administered aspirin antiplatelet therapy. Meanwhile, clopidogrel is preferably administered to patients with allergies to aspirin. Antiplatelet administration for > 65 years old patients should be under a doctor's supervision (Pokdi Stroke PERDOSSI, 2011).

Other short-term preventive actions for recurrent stroke are taking adequate rest, sleeping regularly for 6-8 hours a day, controlling stress by positive thinking, and regularly monitoring risk factors of heart disease, hypertension, dyslipidemia, and diabetes mellitus (DM). Hypertension is controlled by a target blood pressure of 140/90 mmHg. The target blood pressure of diabetes mellitus or chronic kidney disease is 130/80 mmHg. The target of blood sugar control levels in diabetes mellitus patients is HbA1C < 7%. The cholesterol levels of people with dyslipidemia can be controlled by performing diet and taking fat-lowering drugs. The target of LDL cholesterol levels is < 100 mg/dl. However, patients with a high risk of stroke should set the LDL cholesterol target of < 70 mg/dl (Pokdi Stroke PERDOSSI, 2011).

(Masruhim, 2016) have revealed that the most widely used type of antiplatelet medicine is aspirin which is found in 35 cases (48.6%), and the antiplatelet therapy of aspirin could more significantly prevent severe cardiovascular incidence than the risk of bleeding. Meanwhile, (Putra et al., 2016) have revealed a relationship between levels of antiplatelet aspirin medication compliance and the incidence of recurrent stroke. Patients with low-moderate compliance levels are at a higher risk of suffering from recurrent stroke than those with a high compliance level (Masruhim, 2016; Putra et al., 2016).

This study suggests several points. Recurrent stroke can be prevented by consuming aspirin. Administration of aspirin for >65 years old patients should be under a doctor's supervision. The administration of a single antiplatelet for patients with comorbid diseases should be monitored. Further research is necessarily conducted to investigate the different times of recurrent stroke in patients who are administered single and combined antiplatelets.

4. Conclusion

This study concludes three major points. The average period of recurrent stroke in patients taking aspirin antiplatelet is 357.88 days. The minimum recurrence time is 93 days, and the maximum recurrence time is 572 days. Meanwhile, the average recurrent stroke period of patients administered to aspirin is between an interval of 138.59 and 185.41 days, and the average duration of taking aspirin is eight months. The average period of recurrent stroke in patients taking clopidogrel antiplatelet is 162 days. The minimum recurrence time is 93 days, and the maximum recurrence time is 572 days. The average recurrent stroke period of patients administered to aspirin is between an interval of 138.59 and 185.41 days, and the average duration of taking aspirin is five months. Finally, there is a significantly different period of stroke recurrence between patients administered to single aspirin antiplatelet and those administered to a single clopidogrel antiplatelet with a ρ-value of 0.000.

Author Contributions: Rahmawati Raising conceived and designed the study. Rahmawati Raising performed all data analyses. Rahmawati Raising, Oktaviarika Dewi Hermawatiningsih, Devi Mariatul Qibtiah, Zaenal Abidin interpreted the results and revised the paper. Adi Permadi wrote the manuscript. All authors read and approved the final manuscript.

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Competing Interests

The authors disclose no conflict.

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