Comparative Pharmacoeconomy and Effectiveness of Combination Antiplatelet Cost in Patient Ischemic Stroke

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Abstract. Stroke is one of the number 3 causes of death in Indonesia which is a cerebrovascular disease and is characterized by brain tissue death that occurs due to reduced blood flow and oxygen to the brain. The effect of ischemia is quite rapid because the brain lacks a supply of glucose and has the ability to anaerobic metabolism. The purpose of this study was to obtain a comparative picture of the cost effectiveness of ischemic stroke therapy with three combination therapy groups. This research is a type of descriptive research with retrospective data collection methods from tracking patient medical records and patient drug costs. The research subjects were 126 patients with a diagnosis of ischemic stroke who were hospitalized during January 2018 to June 2019 who met the inclusion criteria and were divided into three groups where the first group (K1) was a group of patients who received a combination of clopidogrel-aspirin antiplatelet, the second group (K2) is a group of patients who receive a combination of DA-clopidogrel-defibrogenating agent and third group (K3) who receive three types of drugs namely, clopidogrel, aspirin and Defibrogenating Agent (D®). Analysis of the effectiveness data in this study was based on the percentage of research subjects who had experienced a decrease in blood pressure during hospitalization. K1 combination therapy reached 67.62% with an average duration of hospitalization of 5.2 days and an average drug cost of Rp 14,063.31. K2 reached 83.33% with an average duration of hospitalization of 4 days and an average drug cost of Rp 117,521. K3 reaches 100% with an average duration of hospitalization of 5.7 days and an average cost of medication Rp 159,048. Second group antiplatelet combination therapy is more cost effective, because the duration of hospitalization is shorter and the target of reducing blood pressure achieved is more optimal.

1. Introduction
As the third highest cause of death after heart disease and cancer, stroke prevalence has been increase annually. Moreover, stroke is the main cause of inability. The prevalence of stroke was increase from 2.68 to 3.05 per 1,000 hemorrhagic stroke and from 5.58 to 9.36 per 1,000 nonhemorrhagic stroke. A comparison study of aspirin versus aspirin plus clopidogrel for stroke prevention showed that aspirin monotherapy was cost-effective. Recently, aspirin has become the drug of choice for stroke management [1].

The cost of treatment on stroke managements remains high. This is one of the main problems in stroke managements. In the United States, treatment cost for stroke patients was $18.8 billion in 2008, and the burden related to inability and early death was $15.5 billion. The objective of this study was to explore the cost effectiveness of combination therapy aspirin klopidogrel, compared to aspirin and defibrogenating agent, and aspirin, clopidogrel, defibrogenating agent on stroke ischemic management.
2. Methodes
This research was conducted at the Ciamis Regional General Hospital. The blood pressure recorded in the medical record is documented on the data collection sheet for analysis on the use of all three groups of combination therapy. The cost of antiplatelet drug therapy that is calculated is the direct medical costs from the acquisition of a financial database at a pharmaceutical installation to be compared, from the effectiveness seen from a decrease in blood pressure and the amount of the cost, as long as the patient is hospitalized. The research subjects were 126 patients with a diagnosis of ischemic stroke who were hospitalized during January 2018 to June 2019 who met the inclusion criteria and were divided into three groups where the first group (K1) was a group of patients who received a combination of clopidogrel-aspirin antiplatelet, the second group (K2) is a group of patients who receive a combination of DA-clopidogrel-defibrogenating agent and third group (K3) who receive three types of drugs namely, clopidogrel, aspirin and Defibrogenating Agent (D®). The method used in this study was retrospectively tracking patient medical records and patient medication costs documented on the data collection sheet. Inclusion criteria in this study included adult patients aged 18 years and over, who were diagnosed with ischemic stroke by a doctor and received combination therapy. The analysis was carried out by calculating direct drug costs to achieve a reduction in blood pressure in patients during hospitalization.

3. Result and Discussion
3.1. Patient characteristics
From 126 stroke ischemic patients which are eligible 83.3% (105 patients) were treated with aspirin combine with klopidogrel, 9.52% (12 patients) aspirin combine with defibrogenating agent and 7.14% (9 patients) aspirin combine with defibrogenating agent and clopidogrel for the other (patients). Stroke patient age between 18 until 60 years old was 30.1% (38 patients) and more than 60 years old in Ciamis Public Hospital was 69.8% (88 patients) as seen at figure 1. This result might be caused by many factors such as life style, activity and environment. More than half of the stroke patients are male (66.6%). The result was similar to Goldstein (2011) that prevalence of stroke in man was higher than women for hemorrhagic or non-hemorrhagic stroke [2]. The effectiveness in this study is the success of the drug to treat blood pressure in ischemic stroke until a reduction in blood pressure is achieved within the duration of the hospitalization day observed in the medical record.

![Age of Patients](image)

**Figure 1.** Patient characteristics based on age (n=126) Series 1, 18-60 years old, series 2 more than 60 years old.

Old age above 60 years according to WHO provisions, is a risk factor for ischemic stroke [3]. This may be due to the start of decreased organ function, including the possibility of atherosclerosis in the blood vessels of patients so that it triggers hypertension which is a risk factor for stroke.
Prevalence of stroke in man was higher than women for hemorrhagic or non-hemorrhagic stroke, this may cause from hormonal factor, activity and occupation.

3.2. Cost description in stroke ischemic patients in Ciamis public hospital

Generally, almost all of cost for stroke ischemic patient in combined therapy with defibrogenating agent group was higher than another group without it. The total cost of treatment in stroke patient in aspirin, klopidogrel, defibrogenating agent group also known as K3 (IDR 159048) was higher than klopidogrel, defibrogenating agent Group (K2) (IDR 117521) and aspirin, klopidogrel group(K1) (IDR 14063) (figure 4).

Figure 2. Patient characteristics by sex (n=126) Series 1 is males and series 2 female

Figure 3. Decreased Blood Pressure VS Length of Stay Patients (n=126)
Figure 4. Length of stay patients vs combined therapy cost (IDR)

This study has various limitations so that further research is needed using different more accurate methods. Several factors can influence and should be further criticized in further research between drug interactions, the actual patient's condition, the presence of pain.

4. Conclusion
Klopidakogrel and defibrinogenating agent combined therapy (K2) for ischemic stroke give shorter Length of Stay (average 4 day), and less costly than K3, we conclude that combination therapy is more cost effective because 83.33% achieved the target of reducing blood pressure compared to another combination therapy in treating ischemic stroke patients in Ciamis Public Hospital.

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