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by Mulyadi Djojosaputro, Christina Roseville Lasma Aritonang

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Research Article

Overview of Anti-platelet Drug Use in Ischemic Stroke Patients at UKI General Hospital in 2015

Mulyadi Djojosaputro[1]*, Christina Roseville Lasma Aritonang[2]

[1] Department of Pharmacology and Therapy, Medical Faculty, Univeristas Kristen Indonesia, Jakarta

[2] Department of Neurology, Faculty of Medicine, Universitas Kristen Indonesia, Jakarta

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*Address for Correspondence:

Mulyadi Djojosaputro, Department of Pharmacology and Therapy, Medical Faculty, Univeristas Kristen Indonesia, Jakarta

Abstract

Stroke is an acute neuro-deficit disease that occurs when there is a disturbance of cerebral blood flow. There are two kinds of stroke, hemorrhagic stroke and ischemic stroke. Ischemic stroke is a stroke that occurs due to the formation of thrombosis and emboli. Thrombosis and emboli block the bloodstream in small blood vessels or prominent blood vessels. Drugs that can cause disturbance to the hemostasis mechanism, such as antiplatelets, are usually used on stroke management. This study aims to know the types and amounts of antiplatelet drugs used on stroke ischemic patients in UKI General Hospital from January to December 2015. This research showed that stroke ischemic occurs more often at age 61 -70 (43%). There are no significant differences between both genders, the most common drugs are Aspilet 80 mg (22 times). For combination drugs, Clopidogrel with Aspilet is used more often than Clopidogrel with Ascardia.

Keywords: stroke, thrombosis, antiplatelet

INTRODUCTION

Stroke is an acute neurological deficit disease caused by a sudden disruption of the brain's blood vessels and can cause disability or death. There are two types of stroke, namely ischemic stroke and hemorrhagic stroke. Ischemic stroke is a stroke that occurs more often than hemorrhagic stroke [1]. Ischemic stroke is a clinical sign of dysfunction or damage to brain tissue caused by reduced blood flow to the brain, disrupting the supply of blood and oxygen demand in brain tissue. This phenomenon is caused by forming a thrombus or embolism in a blood vessel and disrupts cerebral blood flow or cerebral blood flow. At the same time, hemorrhagic stroke is a disease of acute, focal or global brain functional disorders due to obstruction of blood flow to the brain caused by cerebral artery bleeding. Blood that comes out of blood vessels can enter the brain tissue, resulting in a hematoma that covers the spaces in the brain [1].

There are four ways to prevent ischemic stroke. The first is to prevent the occurrence of stroke risk factors for individuals who do not have risk factors, and the second is to reduce the incidence of stroke risk factors for individuals who have risk factors by implementing a stroke-free healthy lifestyle, third is to treat stroke patients so that stroke does not continue, and the fourth is for those who have suffered a stroke so that the paralysis experienced does not worsen and reduces dependence on others in daily life activities by participating in physical, mental or social rehabilitation [2; 3].

The prevention process has a significant role in looking at the high risk of stroke. Nevertheless, prompt and appropriate management is equally essential for those who have had a stroke considering that stroke has a high risk of disability and death. By looking at the causes of stroke, the goals of stroke management are to quickly restore blood flow to the blocked brain, reduce disability and death rates, prevent re-occlusion and prevent recurrent strokes.

The third stage of prevention is intended for those who have suffered a stroke. At this stage, the emphasis is on treating stroke patients so that stroke does not continue to become chronic. The actions taken were [2]: a) cetosal (acetylsalicylic acid) was used as the first choice of antiplatelet anti-aggregation drug with doses ranging from 80-320 mg/day, oral anticoagulants were given to patients with risk factors for heart disease (atrial fibrillation, myocardial infarction). Acute, valvular disorders), and other coagulopathic conditions; b) Clopidogrel at a dose of 1x75 mg; and c) Lifestyle modification and stroke risk factors, for example, taking appropriate antihypertensive drugs in patients with hypertension, taking hypoglycemic drugs in diabetics, low-fat diet and taking antidyslipidemic drugs in patients with dyslipidemia, quitting smoking, quitting alcohol, avoiding being overweight and lack of movement.

Handling stroke requires sacrifices that are not small, both from the moral and material aspects of every family who faces this problem. Therefore, risk assessment in patients with stroke should be considered. Every stroke patient needs to be informed about the risk factors that may be owned by the patient's immediate family so that an initial examination can be carried out on the patient's close family.

Considering factors are thought to be associated with the rate of use of antiplatelet drugs in stroke patients, especially ischemic stroke. Researchers are encouraged to conduct this study to know the description of the use of these drugs in ischemic stroke patients at the UKI General Hospital for the period January - December 2015.

The problem in this study is how the description of the use of antiplatelet drugs in ischemic stroke patients at the UKI General Hospital for the period January - December 2015. To know the description of antiplatelet drugs in ischemic stroke patients at the UKI General Hospital for the January - December period. December 2015.

Literature Review

Stroke is an acute neurological deficit disease caused by brain blood vessel disorders that occur suddenly and can cause disability or death [4]. Stroke is a clinical sign that develops rapidly due to focal (or global) disturbances with symptoms lasting 24 hours or more and can lead to death without any apparent cause other than vascular [1; 5]. Stroke can be divided into two main categories: ischemic stroke and hemorrhagic stroke. Approximately 80% of strokes are due to ischemic cerebral infarction, and 20% to cerebral haemorrhage or stroke due to hemorrhagic [6]. The incidence of stroke increases with age.

Ischemic stroke is a clinical sign of dysfunction or damage to brain tissue caused by reduced blood flow to the brain, thereby disrupting the need for blood and oxygen in brain tissue. Blockage of blood flow to the brain can be caused by clots/thrombus plaques resulting from the atherosclerotic process and the formation of emboli originating from the heart. Hemorrhagic stroke is caused by leakage or rupture of blood vessels in the brain so that blood covers the spaces in the brain. Bleeding can occur into brain tissue (called intracerebral haemorrhage or intracerebral hematoma) or into the subarachnoid space, which is the narrow space between the surface of the brain and the layer of tissue that covers the brain (called subarachnoid haemorrhage). It is the most lethal type of stroke and accounts for a fraction of the total stroke, i.e. 10-15% for intracerebral haemorrhage and about 5% for subarachnoid haemorrhage [7].

Hemorrhagic stroke is divided into a) intracerebral haemorrhage (ICH) 2; b) Subarachnoidal haemorrhage (PSA) [8]; and c) Subdural haemorrhage. Ischemic strokes can appear suddenly. The main sign seen is that there is a focal neurologic deficit. New symptoms occur within seconds or minutes or occur when you wake up. The deficit may improve rapidly, be progressively worse, or persist. Symptoms that can be found [9]: a) There is an attack of neurological deficits, such as hemiparesis (paralysis on the right or left side of the body); b) Difficulty hearing, seeing, swallowing, walking, writing, reading, and understanding writing; c) loss of balance or coordination; d) sudden headache with no apparent cause; e) A slurred mouth or protruding tongue, Difficulty speaking or speaking fluently and difficult to understand other people's speech; and f) Nausea and vomiting occur, particularly strokes affecting the brainstem and cerebellum.

The brain is a complex human organ. Each area of the brain has a particular function, such as moving, thinking, seeing, etc. The brain needs much oxygen to function correctly. The brain's weight is only 2.5% of the total body weight, but the oxygen needed is almost 20% of the total body needs [10]. This oxygen is obtained from the blood. Under normal circumstances, Cerebral Blood Flow or blood flowing to the brain is 50-60 ml/100 g brain/minute [11].

The brain gets blood from arteries. The first is the internal carotid artery which consists of the carotid arteries (right and left), which supply blood to the front of the brain called the anterior cerebral artery circulation. The second is the vertebral column, which supplies blood to the back of the brain, referred to as the posterior cerebral artery circulation. Furthermore, the anterior cerebral artery circulation meets the posterior cerebral artery circulation to form a circle of Willis [12; 3]. There are two hemispheres in the brain that have each function. The functions of the brain is a movement or motor centre, as a sensibility centre, as a motor speech centre or Broca's area, as a sensory speech centre or Wernicke's area, as a visuosensory area, and the cerebellum, which functions as a coordination centre and the brainstem which is the brain stem. The site of the pathway of nerve fibres to the target organ [6].

Platelets are non-nucleated blood cells derived from the cytoplasm of megakaryocytes. Platelet life ranges from 7-to 10 days. These cells play an important role in hemostasis because platelets form a hemostatic plug to close the wound. Without platelets, spontaneous blood leakage can occur through small blood vessels. The hemostatic plug formation occurs through several stages, namely adhesion, activation, and aggregation. The normal value of platelets in adults is 150,000–400,000 cells/mm3 while in children 150,000–450,000 cells/mm3 [13]. Thrombopoietin is a major regulator of platelet production, produced by the liver and kidneys [14]. There are studies that blockage blood vessels in the brain and heart often occurs due to hyperactivity of platelet function. This hyperactivity of platelets increases the ability of platelets to clot and will cause thrombosis, which can clog blood vessels. Platelets are shaped like a biconvex disc with a 2-4 m diameter and a 7-8 fl volume in the inactive state. The external sheath of platelets is thicker and denser than cells and contains many glycoproteins that function as receptors. Glycoprotein I and V are receptors for thrombin, glycoprotein Ib is a receptor for Von Willebrand factor, while glycoprotein II b and III a are receptors for fibrinogen.

With electron microscopy, platelets can be divided into four zones, each zone having a specific function. The peripheral zone is helpful for adhesion and aggregation, and the sol-gel zone supports the structure and mechanism of contraction, the organelle zone, which plays a role in the discharge of platelet contents and the membrane zone that comes out of the contents of granola during release [15]. The organelle zone consists of dense granules, mitochondria, granules and organelles (lysosomes and endoplasmic reticulum). Dense granules contain and release the nucleotides adenine, serotonin, catecholamines and platelet factor. While the granules contain and release fibrinogen, PDGF (platelet-derived growth factor), lysosomal enzymes.

The adhesion process is the attachment of platelets to blood vessels. Platelet adhesion involves an interaction between platelet membrane glycoproteins and exposed or injured tissue. Platelet adhesion is dependent on a plasma protein factor called the von Willebrand factor. Platelet adhesion is associated with increased adhesion of platelets so that platelets adhere to each other and endothelium or injured tissue and thus, a primary hemostatic plug is formed [14; 16].

Activated platelets can synthesise prostanoids, most notably thromboxane A2 from arachidonic acid, which is released from membrane phospholipids via activation of phospholipases, cyclooxygenase (COX-1) and TX synthase. The induced form of COX (COX-2) is not only found in vascular endothelium and monocytes but is found in newly formed platelets, accelerating the process of platelet production [17]. Platelets have cohesion with each other due to the influence of ADP and thromboxane A2. This cohesion is called the platelet aggregation function. The release of ADP and thromboxane A2

causes the existing platelets to aggregate at the site of vascular injury. ADP causes platelets to swell and makes it easier for the membranes of adjacent platelets to stick together. Thromboxane A2 is also a solid vasoconstrictor to prevent further ejection of blood from damaged vessels. This process will continue to form a large enough platelet mass to occlude the endothelial wound area [18].

Platelet aggregation examination evaluates platelet function, especially in patients with average platelet counts but accompanied by bleeding or patients with normal platelets with a tendency to thrombosis. Platelet aggregation test is one way to determine the benefits of aspirin in ischemic stroke patients. The examination can be done macroscopically, microscopically, and analyser, but the analyser is most commonly used. The tests performed evaluated changes in light emission due to aggregation arising in platelet-rich plasma (PRP) arising from stimulation by platelet agonists such as ADP [19].

Antiplatelet Aspirin or acetylsalicylic acid (ASA) belongs to the class of non-steroidal anti-inflammatory drugs (NSAIDs) or non-steroidal anti-inflammatory drugs (NSAIDs), which function as analgesics (pain relievers), antipyretics (fever reducers) and anti-inflammatory (anti-inflammatory). Aspirin has been recommended to treat stroke and transient ischemic attack to reduce the risk of recurrent stroke, myocardial infarction and death from vascular disorders by 22%. Aspirin was the first drug used to prevent stroke, but now it has begun to be used with other antiplatelet drugs such as clopidogrel.

Aspirin is an antiplatelet agent evaluated for the treatment of acute ischemic stroke. Aspirin works by inhibiting the cyclooxygenase enzyme, which plays an essential role in arachidonic acid metabolism. Inhibition of this cyclooxygenase enzyme occurs in platelet cells and blood vessel walls so that the formation of prostacyclin (PGI2) and thromboxane A2 will be disrupted. The mechanism of inhibition of the cyclooxygenase enzyme by aspirin occurs by acetylase. Because platelets cannot regenerate against cyclooxygenase, the effect of aspirin is over the lifespan of platelets (generally ten days) [20].

Aspirin has two opposing effects on platelet aggregation. However, platelet cyclooxygenase is more sensitive to aspirin blockade than blood vessel wall cyclooxygenase. Low-dose aspirin administration will selectively inhibit platelet cyclooxygenase. Thereby inhibiting the formation of thromboxane A2 but not inhibiting blood vessel wall cyclooxygenase so that prostacyclin will still be formed. Thus, at low doses, aspirin will have an antiplatelet aggregation effect, whereas, at high doses, it inhibits the formation of thromboxane A2 and inhibits the formation of prostacyclin so that it does not have an anti-aggregation effect. Because platelets synthesise little protein during their lifetime, inhibition of the cyclooxygenase enzyme lasts as long as the platelets live. Thus a single therapeutic dose will result in one week of platelet breakdown. Aspirin is absorbed rapidly and practically wholly, especially in the first part of the duodenum. However, because it is acidic, some substances are also absorbed into the stomach. Aspirin is absorbed intact hydrolysed to salicylic acid, mainly in the liver [21]. For decades, antiplatelet therapy has focused on the thromboxane pathway, and this pathway is inhibited by aspirin. The dose often used is 75-325 mg/day because this dose is considered quite effective and has fewer bleeding side effects than higher doses.

Giving aspirin is indicated in patients with chest pain complaints due to blockage in the heart arteries a history of recurrent ischemic stroke. Aspirin can also reduce headaches, toothaches and reduce symptoms of influenza, fever, and muscle aches. Aspirin should not be administered to patients with known hypersensitivity reactions to NSAIDs, active peptic ulcer, severe cardiac and renal dysfunction, pregnancy in the third trimester and use in children under 16 years is not recommended [23]. Side effects of aspirin: a) Allergies in the form of hives to Steven-Johnsons syndrome; b) Asthma attacks and shortness of breath; c) Discomfort in the stomach; d) Spontaneous bleeding and gastrointestinal bleeding; and e) Impaired liver and kidney function.

Table 1: Lowest and Most Effective Dose of Aspirin [22]

Abnormalities	Dosage per day (mg)
Transient ischemic attack and ischemic stroke	50
Patients at high risk of cardiovascular disease	75
Hypertension	75
Stable angina pectoris	75
Unstable angina pectoris	75
Carotid artery stenosis	75
Polycythemia vera	100
Acute myocardial infarction	160
Acute ischemic stroke	160

Non-steroidal anti-inflammatory drugs (NSAIDs), including aspirin, can cause bleeding because the drug crystals directly contact the gastric mucosa. Aspirin damages the gastric mucosa, thereby altering the permeability of the epithelial barrier, allowing back diffusion of hydrochloric acid with consequent tissue damage, especially blood vessels. Histamine has released the secretion of acid and pepsin, and several plasma proteins can be lost so that the capillary mucosa can be damaged and bleeding. The risk of gastric bleeding caused by NSAID drugs depends on the dose of the drug used, where this risk increases complications in patients with long-term drug use [3].

Clopidogrel belongs to the thienopyridine class of drugs. Clopidogrel is a second-generation antiplatelet aggregation drug. Ticlopidine, a first-generation antiplatelet aggregation drug, is no longer used because it can cause bone marrow toxicity. Clopidogrel has a limitation in that it has a slower onset of action than Prasurgel, a third-generation antiplatelet aggregation drug with a faster onset of action and more consistent platelet inhibition. All three thienopyridine drugs are prodrugs. Before being active, these drugs must pass through metabolic processes in the hepatic CYP450 system to active substances that will inhibit platelet P2Y12 receptors.

Clopidogrel is also used in patients who have contraindications to aspirin. Clopidogrel selectively inhibits the binding of adenosine diphosphate (ADP) to the P2Y12 ADP receptor on platelets, thereby inhibiting ADP-mediated activation of the glycoprotein GPIIb/IIIa complex, which ultimately induces an inhibitory reaction to platelet aggregation [24]. Clopidogrel also inhibits platelet aggregation induced by other agonists by blocking the development of platelet activation by releasing ADP. Clopidogrel acts by irreversibly modifying the platelet ADP receptor. As a result, platelets exposed to clopidogrel are affected for the remainder of their lifespan.

After repeated administration of 75 mg daily, clopidogrel is rapidly absorbed. However, the plasma concentration of the parent compound was shallow and below the quantification limit (0.00025 mg/l) after 2 hours of administration. Absorption of at least 50% is based on urinary excretion of the Clopidogrel metabolite. The liver rapidly metabolises clopidogrel and the primary metabolite, the inactive one, is a carboxylic acid derivative, representing about 85% of the

compound circulating in plasma. This metabolite's peak plasma levels (about three mg/l after repeated 75 mg oral doses) occur about 1 hour after dosing. Clopidogrel should be given as a single daily dose of 75 mg with or without food. Patients with acute coronary syndromes: a) Non-ST segment elevation (unstable angina or non-Q-wave myocardial infarction); and b) ST-segment elevation of acute myocardial infarction.

Prolonged use of clopidogrel may increase the risk of bleeding and unwanted haematological effects. Therefore, determining blood cell counts and other appropriate tests should be considered immediately if clinical symptoms suggestive of bleeding develop during treatment. Clopidogrel should be cautioned in patients receiving treatment with aspirin, NSAIDs, COX-2 inhibitors, heparin or glycoprotein IIb/IIa. In addition to bleeding in the gastrointestinal tract, possible side effects are purpura, bruising, hematoma, epistaxis, haematuria, ocular haemorrhage, intracranial bleeding, abdominal pain, gastritis, constipation, rash, and pruritus (itching).

RESEARCH METHOD

This study used a descriptive method with a retrospective research design. Sampling was carried out using medical records at UKI General Hospital. Data collection will be carried out in October - December 2016. This study used secondary data, namely medical records of outpatients for neurological diseases at UKI General Hospital in January-December 2015. The population in this study was all stroke patients at UKI General Hospital for January - to December 2015. 2015. In this study, the samples used were all ischemic stroke patients at UKI General Hospital from January 2015 - to December 2015 who met the inclusion criteria. The sampling technique used is random sampling, a method of selecting a sample size from a population where each member of the population has the same opportunity, and all possible combinations selected as samples have the same. The data collected came from the medical records of inpatients with neurological diseases at UKI General Hospital from January to December 2015 who entered the inclusion criteria. The inclusion criteria were all ischemic stroke patients who used antiplatelet drugs. The data collected will be grouped by type of stroke and then statistically processed using the Statistical Product and Service Solution (SPSS) program. This study follows the rules following applicable research ethics by keeping the identities of existing patients confidential. Documents regarding identity and data related to research on hypertension profiles in ischemic stroke patients are only used for research purposes.

RESULT AND DISCUSSION

This section presents data on ischemic stroke patients through medical records at UKI General Hospital from January 2015 - to December 2015. After going through the data collection process, only 100 patients were included in the author's criteria out of 423 people. The data are presented in the tabulated and narrated form about the description of age, gender, and description of the use of antiplatelet drugs.

Table 2: Gender Profile of Ischemic Stroke Patients

Sex	N	%
male	51	51
female	49	49
Total	100	100

The sex profile of the patients included in the authors' criteria did not have a significant difference between men (51%) and women (49%) out of a total of 100 patients.

Table 3: Description of the Age of Ischemic Stroke Patients

Age	N	%
<40	2	2
41-50	3	3
51-60	37	37
61-70	43	43
71-80	13	13
>80	2	2
Total	100	100

The description of the age of the patients in the study was divided into six age groups. Most patients who entered the study criteria had an age range between 61-70 years, 43 of 100 patients or 43% of the total sample. At the same time, patients with age groups aged below 40 years and above 80 years were the least with the number of 2 people or equivalent to 2% of the total sample.

Table 4: Overview of Anti Platelet Drugs

Types of Anti Platelet Drugs	N	%
As aspirin 80mg	22	22
Aspilet 160mg	3	3
Ascardia 80mg	14	14
Ascardia 160mg	4	4
Miniaspi 80mg	5	5
Clopidogrel 75mg	3	3
Aspilet, Ascardia	5	5
Aspilet, Ascardia, Miniaspi	2	2
Ascardia, Miniaspi	6	6
Aspilet, Miniaspi	10	10
Aspilet + Clopidogrel	9	9
Ascardia + Clopidogrel	7	7
Aspilet, Miniaspi + Clopidogrel	2	2
Miniaspi + Clopidogrel	2	2
Ascardia, Miniaspi + Clopidogrel	4	4
Thromboaspilet, Ascardia	2	2
Total	100	100

Types of Anti Platelet Drugs	N	%
Acetosal	73	73
Clopidogrel	3	3
Acetosal + Clopidogrel	24	24
Total	100	100

The results showed that the antiplatelet drug most often given to ischemic stroke patients was Aspilet 80 mg, with a total of 22. For the combination drug with clopidogrel, the most frequently used drug was Aspilet 80 mg with 9, followed by Ascardia with several 7. In table 4.1, it can be seen that between men and women, there is no significant difference. Out of 100 outpatients at UKI General Hospital, 51 patients (51%) were male, and 49 patients (49%) were female.

However, according to a study, men have a greater tendency to have an ischemic stroke than women, with a ratio of 2:1. Women have estrogen and progesterone hormones, which can protect them from heart disease and stroke, but women will catch up after they reach menopause [26]. In the results of this study, most ischemic stroke patients were aged 60-71 years. Table 3 above shows that out of 100 outpatients at UKI General Hospital, 43 patients (43%) were aged 60-71 years, followed by patients aged 51-60 as many as 37 patients (37%).

Age is the most critical risk factor for all strokes. The incidence of stroke increases with age. After 55 years, the risk of ischemic stroke can increase 2-fold. As we know, blood vessels in older people tend to undergo degenerative changes and begin to be seen due to the atherosclerosis process. Sooner or later, this process can trigger a stroke depending on a healthy lifestyle and a person's behaviour and diet. Antiplatelet aggregation drugs used in Indonesia are acetylsalicylic acid (acetosal), clopidogrel and cilostazol [27]. This study found that Aspilet 80 mg acetosal was the most frequently used antiplatelet aggregation drug in ischemic stroke patients as many as 22 patients (22%). It could be due to the availability of Aspilet at UKI General Hospital, which was more than Ascardia and Miniaspi. In addition, the price of Aspilet is also more affordable to the public. Acetosal is an NSAID class drug so long-term use can increase the risk of gastrointestinal bleeding.

Asgardian is enteric-coated acetosal, meaning that the drug is coated with a material that is relatively insoluble in gastric acid but can be dissolved in an alkaline environment in the small intestine and frees the drug contained in it so that it is relatively safe for the stomach compared to ordinary acetosal. There is a study of patients who used acetosal for a long time. On gastric endoscopy, it was seen that 90% of patients who used plain acetosal had erosion of the gastric mucosa, while only 60% of patients used enteric-coated acetosal. This study can conclude that enteric-coated acetosal can reduce the risk of gastrointestinal bleeding compared to plain acetosal. Fourteen patients (14%) used Ascardia 80mg at UKI General Hospital.

Clopidogrel alone can be used as a substitute if the patient has contraindications to aspirin. The use of clopidogrel should also be considered in patients taking proton pump inhibitor drugs because the interaction of clopidogrel with PPIs can reduce the effectiveness of clopidogrel in inhibiting platelet aggregation [28]. This study found that only three patients (3%) were taking clopidogrel as an antiplatelet drug alone.

Clopidogrel can also be combined with acetosal. According to a study conducted on patients with transient ischemic attack or mild ischemic stroke, the addition of clopidogrel with aspirin within 24 hours of symptom onset reduced the risk of further stroke by 32%, compared to taking acetosal alone. However, this combination may increase the risk of gastrointestinal bleeding even if only minor bleeding [29].

In this study, 24 patients (24%) used the combination drug acetosal and clopidogrel. Acetosal Aspilet 80mg was the most combined in 9 patients (9%), followed by Ascardia 80mg in 7 patients (7%).

CONCLUSION

Based on the study results describing the use of antiplatelet drugs in ischemic stroke patients at the UKI General Hospital in 2015. It was found: a) Gender distribution in ischemic stroke patients was more common in male patients than female patients because women have progesterone and estrogen hormones that function as protection against heart disease and stroke; b) Age distribution in ischemic stroke patients is more common in patients in the age range of 61-70 years. It could be due to the increased risk of stroke for women who have experienced menopause, which usually occurs at the age of 50 years and over; c) The distribution of the most antiplatelet drugs given to ischemic stroke patients at UKI General Hospital in 2015 was Aspilet 80 mg acetosal as many as 22 patients followed by Ascardia 80 mg as many as 14 people. It could be due to the availability of antiplatelet drugs at UKI General Hospital in 2015. In conclusion, Ascardia is a better antiplatelet drug because Ascardia is an enteric-coated acetosal drug, Ascardia has a protective or coating that functions as a gastric protector compared to Aspilet, which is plain acetosal; and d) 24 patients were given a combination of acetosal and clopidogrel, nine patients used aspirin 80 mg of aspirin with clopidogrel. Combining these two types of drugs can reduce the risk of further stroke more effectively than single drug administration. However, long-term use can increase the risk of gastric bleeding, although not significantly.

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