

The Relationship between Drug-Related Problems and Clinical Outcomes in Ischemic Stroke Patients in the Hospitalized Neurology Ward of RSUP Dr. M. Djamil Padang

Sri Rahmi Utami¹, Suhatri², Yelly Oktavia Sari³

Magister Pharmacy, Faculty of Pharmacy, Andalas University Padang, Indonesia

Abstract:- This Stroke is the third leading cause of death globally after cardiovascular disease and cancer. The highest death rate in Indonesia is caused by stroke (21.2%), and data from the Indonesian Ministry of Health reports that stroke is the highest cause of death in Indonesia, which is 51%. Stroke patients who are hospitalized generally experience drug-related problems (DRPs), especially patients with complications and comorbidities. This study aims to determine the types of DRPs and the relationship between DRPs and Clinical Outcomes in ischemic stroke patients in the inpatient neurology ward of RSUP Dr. M. Djamil Padang. This study is an observational study using a descriptive cross-sectional design, conducted by collecting data on ischemic stroke patients prospectively during the period May – July 2019. Data analysis used statistics using parametric test methods (T- Test and One Way Annova) and non-parametric test methods (Mann U Whitney and Kruskal Wallis Test). It was found that the most used drugs in stroke patients were antihypertensive drugs; amlodipine (class Ca Chanel Blocker) and candesartan (class Angiotensin Receptor Blocker), antiplatelet drugs; aspirin, H2 antagonist drugs; ranitidine, an antibacterial drug; ceftriaxone, a mucolytic drug; N – acetylcysteine and body fluids; stranger. For the types of Drug-Related Problems, namely drugs without indications at 14.29%, indications that are not treated by 59.52%, inappropriate drug selection by 16.47 %, excess doses by 0%, under doses by 2.38%, side effect reactions are 0%, drug interactions are 7.14%, and failure to receive drugs is 0%. From the results of statistical tests, it was found that there was a relationship between Drug- Related Problems in the inappropriate drug category and drug interactions with Clinical Outcomes of patients with systolic blood pressure. Then, there was a relationship between Drug-Related Problems in the category of drugs without the Clinical Outcomes score of patients with the Glasgow Coma Scale.

Keywords:- Clinical Outcomes; DRPs; Ischemic Stroke; Ischemic Stroke Therapy).

I. INTRODUCTION

Stroke is the third leading cause of death globally after cardiovascular disease and cancer. Stroke has been recorded more than 700,000 per year with a mortality rate of 150,000. The impact of this disease can cause physical and mental disabilities due to blockage or bleeding of blood flow to the brain, which causes acute neurologic damage. The highest death rate in Indonesia is caused by stroke (21.2%) and followed by heart disease (8.9%), diabetes mellitus (6.5%), respiratory tract infections (5.2%), tuberculosis (4.3%⁹, and other infectious diseases.¹ In addition, the Indonesian Ministry of Health reports that stroke is the highest cause of death in Indonesia, in 51%.²

There are three keys to the management of stroke patients, namely (1) preventing neurological damage and patient disability, (2) preventing worsening and limitation of patient movement (immobility), and (3) preventing stroke recurrence.

Most stroke patients will receive more than three kinds of drugs for first aid because stroke patients have comorbidities and/or complications. Multidisciplinary cooperation is needed by doctors, nurses, pharmacists and other health workers, and even patients' families to achieve good therapeutic outcomes in stroke patients.³

Stroke patients who are hospitalized generally experience drug-related problems (DRPs), especially patients with complications and comorbidities. Therefore, pharmacists have an essential role in ensuring the treatment of stroke patients by identifying DRPs, both potential and actual conditions. However, there has been a shift in the role of pharmacy to be more patient-oriented than drug-oriented in the health care system. Clinical outcomes of patients are clinical outcomes of patients after receiving treatment and are indicated by GCS, blood pressure, motor, and discharge conditions, such as improvement or death of ischemic stroke patients as a determinant of the success of therapy.

This study aimed to determine the types of DRPs in ischemic stroke patients and to analyze the relationship between DRPs and Clinical Outcomes in ischemic stroke patients in the inpatient neurology ward of RSUP Dr. M. Djamil Padang. At this hospital, stroke is one of the most common diseases in the inpatient neurological ward, where the average stroke patient in the neurological ward is

hospitalized for 12 days.²

II. METHOD

A. Research Design

The study was collected in an observational manner with a descriptive cross-sectional design by collecting data on ischemic stroke patients prospectively during the period April- July 2019. With the Certificate of Passing the Ethical Review no. 186/KEPK/2019 issued by the Health Research Ethics Committee RSUP Dr. M. Djamil Padang.

B. Sampling

The criteria included all ischemic stroke patients in the inpatient neurology ward, either acute, recurrent, or post-stroke at Dr. RSUP. M. Djamil Padang. Exclusion criteria included ischemic stroke patients hospitalized forcibly and incomplete medical records of patients who received ischemic therapy.

C. Data

The data was obtained through the recording of medical records in the neurological ward of RSUP Dr. M. Djamil Padang, covering qualitative and quantitative data as well as the completeness of patient data (such as age, gender, history of current illness, history of previous illness, family history, previous drug history, therapeutic measures for ischemic stroke, diagnosis, physical examination, examination support, etc.). The data taken is transferred to a data collection sheet (worksheet) that has been prepared. Lack of medical records is complemented by looking at nurse records, drug records at the neurology pharmacy depot, seeing the patient's condition directly, and asking questions to the patient or patient's family.

D. Data Analysis

Data on general characteristics of ischemic stroke patients including age, gender, length of stay, comorbidities, and data on the use of drugs for therapy of stroke patients were collected and then calculated the number and percentage.

Data intake from medical records, nurse records, list of drug use, laboratory data, and patient conditions, then make a table of patient data sheets and tables of patient treatment datasheets. Furthermore, it is analyzed according to the category of Drug-Related Problems experienced by patients by looking at the standard of therapy at Dr. RSUP. M. Djamil, Guideline or other scientific literaturess. The data for each category of DRPs were then added up, and the percentage was calculated, then analyzed the relationship between DRPs and the patient's Clinical Outcomes with statistical analysis (T-test statistical test, One Way Annova, Mann Whitney U and Kruskal Wallis Test.

III. RESULTS

Based on the research that has been done at RSUP, Dr. M. Djamil Padang, from April - to July 2019, found the number of ischemic stroke patients treated in the neurology ward to as many as 80 people. And there are 72 patient data included in the inclusion criteria, while eight are included in the exclusion criteria, with six patients being forced to go home and two patients with incomplete data.

The sex distribution of 72 ischemic stroke patients who met the inclusion requirements of research subjects was male 34 patients (47.2%), and female 38 patients (52.8%) who were treated in the neurology ward of RSUP Dr. M. Djamil Padang as shown in table 1. Ischemic stroke patients with an age range of 26-35 years were 3 patients (4.2%), aged 36-45 years were 7 patients (9.7%), aged 46-55 years as many as 19 patients (26.4 %), age 56-65 years as many as 20 patients (27.8%) and age over 65 years as many as 23 patients (31.9%). This shows that the prevalence of stroke increases from the age of 55 years and over (Fagan et al., 2017). Meanwhile, based on the length of stay for ischemic stroke patients, 50% of patients were treated for one week, 40.3% of patients were treated for two weeks, 6.9% of patients were treated for three weeks, and 2.8% patients were treated more than 21 days (Table 1).

The most drugs used by doctors in ischemic stroke patients based on disease risk factors are antihypertensive drugs; amlodipine (the Ca Chanel Blocker group) as many as 29 uses (40.3%) and candesartan (the Angiotensin Receptor Blocker group) as many as 33 uses (33.3%) and antiplatelet drugs; aspirin as many as 43 uses (59.7%). While the use of drugs based on comorbidities (not related to risk factors), which is H2 antagonist drugs; ranitidine as many as 59 uses (81.9 %), antibacterial drugs; ceftriaxone as many as 39 uses (54.2 %), mucolytic drugs; N-acetylcysteine as much as 30 uses (41.7 %), and body fluids as much as 55 uses (76.4 %).

Table 1. Sociodemographic Characteristics of Respondents

No	Sociodemographic Characteristics	Number of Patients (n = 72)	Percentage (%)
Sex			
1	Laki – laki	34	47,2
2	Perempuan	38	52,8
Age (Years)¹⁵			
1	17 – 25	0	0
2	26 – 35	3	4,2
3	36 – 45	7	9,7
4	46 – 55	19	26,4
5	56 – 65	20	27,8
6	> 65	23	31,9
Length of Treatment (Days)			
1	1 – 7	50	50,0
2	8 – 14	29	40,3
3	15 – 21	5	6,9
4	>21	2	2,8

IV. DISCUSSION

The research data found that the female suffered the most ischemic stroke because, in women, the risk factor for stroke was possibly influenced by contraceptive drugs. The length of stay for ischemic stroke patients with a mean length of stay between 5 to 25 days can be caused by clinical deterioration after an ischemic stroke attack related to the degree of stenosis or expansion of carotid artery blockage by thrombus.

The percentage of ischemic stroke patients based on comorbidities diagnosed by doctors is shown in table 2 that hypertension is the most common comorbidity found in ischemic stroke patients (71.45%). This causes an increase in blood pressure which is the body's compensatory mechanism to meet the need for blood supply due to the presence of lesions.⁵ The second most common comorbid disease is bronchopneumonia which reaches 30.6%. Pneumonia caused by bacteria is a major complication in acute ischemic stroke patients.⁶

Factors that can influence the occurrence of pneumonia in stroke patients are the severity of the stroke, elderly, male, dysphagia, chronic obstructive pulmonary disease, and coronary artery disease. At the beginning of the occurrence of a stroke followed by an increase in blood sugar levels, it is a compensatory reaction mechanism in the body or due to stress. The rise in blood sugar in stroke patients has the potential to worsen brain damage, so it is necessary.⁵ PERDOSSI (Indonesian Neuroscientist Association) states that hypertension, diabetes mellitus, heart disease, and dyslipidemia are risk factors for stroke.⁸

For the use of drugs in the antihypertensive therapy class because the subjects of this study were stroke patients where the highest risk factor for stroke was hypertension. Antihypertensives are not a priority in therapy within 24 hours of onset. Unless the blood pressure is more than 200/120 mmHg, the patient's blood pressure should be reduced by about 15% by using labetalol, nicardipine, or nitroprusside.^{8,9} To prevent recurrence of stroke for diabetics and kidney disease by managing blood pressure between 140/90 mmHg and less than 130/80 mmHg.¹⁰

Drug-related problems (DRPs) are associated with drug therapy, affecting the actual or potential outcome of a patient's therapy. Management of drug therapy ensures correct dosage, prevents drug interactions, and provides information to patients about possible side effects, especially in patients with various diseases, patients with chronic diseases, and patients receiving multiple drugs.⁹ The results of Drug- Related Problems inpatients in the neurological ward of Dr. RSUP. M. Djamil can be seen in Table 3.

Drugs without indications are drugs that are not needed or that are not in accordance with medical conditions¹¹, and six events (14.63%) were found in 6 ischemic stroke patients because there was the administration of tranexamic acid, but it was not known for what indications based on laboratory

results or diagnosis, patients received KSR (Potassium Chloride) therapy, but the patient's Potassium value was still in the normal range (Potassium = 3.5 – 5.1 Mmol/L) and received candesartan therapy as well, so it could cause hyperkalemia.²⁰

Table 2. Percentage of Number Patients Based on Comorbidities Diagnosed by Doctors

Comorbidities	Number of Patients	Percentage (%) (n = 72)
Hypertension	50	71,5
Broncopneumonia	22	30,6
Diabetes Mellitus	14	19,4
Dyslipidemia	9	12,5
Sepsis	5	6,9
Chronic Kidney Disease	4	5,6
AF NVR (Atrial Fibrilasi Normal Ventricular Response)	4	5,6
Congestive Heart Failure	3	4,2
Atrial Fibrilasi	3	4,2
Anemia	3	4,2
Hipoalbuminemia	3	4,2
Stress Ulcer	3	4,2
Hematemesis Melena	2	2,8
NSTEMI (Non ST Segment Elevation) Myocardial Infarction	2	2,8
Thrombocytopenia	2	2,8
Acute Kidney Injury	2	2,8
Old MCI (Myocard Infarction)	2	2,8
COPD (Chronic Obstructive Pulmonary Disease)	2	2,8
Ulcus Decubitus	2	2,8

Untreated indications are medical conditions of patients who require drug therapy but do not receive drugs, such as requiring combination therapy to obtain synergistic or additive effects, preventive therapy to reduce disease progression¹¹ and found 25 events (60.97%) in 21 ischemic stroke patients. Including not being given antidiabetic drugs, antihyperlipidemic drugs, or antihyperuricemic drugs for the treatment of moderate anemia. Hyperglycemia is mostly experienced by non-diabetic acute stroke patients (60%). Hyperglycemia after acute stroke may worsen the patient's condition because of the associated infarct volume and cortical disturbances. Not much research data states that actively lowering blood sugar levels will improve the patient's condition, where it is better to avoid blood sugar levels exceeding 180 mg/dl.⁸ Antibacterial drugs are intended for the most common medical complication in stroke patients, namely bronchopneumonia, with an estimated incidence in stroke patients between 5% to 26%. Pneumonia caused by bacteria is a significant complication in acute ischemic stroke patients.¹² Patients with ischemic stroke have moderate anemia with hemoglobin values of 7-11 g/dl. Patients with moderate anemia 7 – 11 g/dl should not be given blood transfusions, but other medications such as iron, vitamin B12, folic acid, or erythropoietin can be given.

Table 3. Data on Drug-Related Problems Occuring in Ischemic Stroke Patients

No	DRPs Criteria	Number of events	Percentage (%)	Number of Patients (n = 72)	Percentage (%)
1	Drugs Without Indication	6	14,29	6	8,33
2	Untreated Indications	25	59,52	19	26,39
3	Inappropriate Drug Selection	7	16,47	7	9,72
4	Overdose	0	0	0	0
5	Less Dosage	0	0	0	0
6	Side Effect Reaction	0	0	0	0
7	Drug Interaction	3	7,14	2	2,78
8	Failure to Receive Medication	0	0	0	0
	Total	41	100		

Inappropriate drug selection causes ineffective drug function based on medical conditions or not the most effective drug to treat the disease. ¹¹ Found seven events (17.07%) in 7 ischemic stroke patients who are related to drug selection in ischemic stroke patients with chronic illness, diabetes mellitus, bronchopneumonia, and hypertension.

Drug interaction is the action of a drug that can be changed or influenced by other drugs if given simultaneously¹¹ and found three events (7.32%) in two ischemic stroke patients, when drug interactions with KSR, this drug can cause hyperkalemia in patients when used concurrently¹⁴, and there is an interaction between ACE inhibitors and NSAIDs which can reduce the antihypertensive effect of ramipril and can cause impaired kidney function.

From the research results, there were no incidences of over-dose, under-dose, and adverse reactions. Then it was also known that the patient was being treated in the neurology ward of RSUP. Dr. M. Djamil Padang obtains drugs well where there is a cooperation from nurses, pharmacists, and patient's families in receiving medications for patients being treated. Where failure to receive medication did not occur (0%), it is said to have failed to receive medication. It can assume that a patient has not received medication once while being treated, the patient is included in the category of failing to receive medication. In the neurology ward of Dr. M. Djamil Padang has used a daily dose system where every time you eat, the medicine is divided/plasticized per time of drinking, making it easier for the patient to take medication at any time. The drug is given when taking medicine, such as morning, afternoon, or evening, not at night. Give one time (total) for one day of taking the drug.

Statistical steps in this study first performed a normality test and the results showed that the data were normally distributed only on systolic blood pressure with a p- value > 0.05 (p = 0.120), while for the Glasgow Coma Scale score data, diastolic blood pressure and motor p-values. <0.05, which means that the data is not normally distributed. Furthermore, statistical tests were carried out with the method used based on normally distributed data (parametric) using the T-test and One Way Anova statistical test and based on abnormally distributed data (non-parametric) using the Mann Whitney U and Kruskal Kawalis statistical tests. The relationship is significant/significant if the significant value obtained is P < 0.05.

In this study, it was found that the clinical outcomes of patients improved as many as 68 people with 36 female patients and 32 male patients. At the same time, the clinical outcomes of patients died as many as four patients, with two female patients and two male patients.

As well as the relationship between Drug-Related Problems in the category of drugs without indications with Clinical Outcomes of patients with Glasgow Coma Scale scores with the Mann U Whitney statistical test, p-value =0.028 (p < 0.05), where the presence of drug administration without indications in patients can reduce the Glasgow Coma score. Patient scale. So that the increasing number of DRPs can lead to poor patient outcomes. However, for other DRPs categories, namely untreated indications and insufficient doses, there was no relationship with the patient's Clinical Outcomes (Glasgow Coma Scale, blood pressure (systolic/diastole), motor and discharge conditions (improvement/death)). So that the increasing number of DRPs can lead to poor patient outcomes. However, for other DRPs categories, namely untreated indications and insufficient doses, there was no relationship with the patient's Clinical Outcomes (Glasgow Coma Scale, blood pressure (systolic/diastole), motor and discharge conditions (improvement/death)). So that the increasing number of DRPs can lead to poor patient outcomes. However, for other DRPs categories, namely untreated indications and insufficient doses, there was no relationship with the patient's Clinical Outcomes (Glasgow Coma Scale, blood pressure (systolic/diastole), motor and discharge conditions (improvement/death)).

V. CONCLUSION

From the results of this study, it was found that the most common use of drugs in stroke patients was antihypertensive drugs; amlodipine (class Ca Chanel Blocker) and candesartan (class Angiotensin Receptor Blocker), antiplatelet drugs; aspirin, H2 antagonist drugs; ranitidine, an antibacterial drug; ceftriaxone, a mucolytic drug; N – acetylcysteine and body fluids; stranger. For the types of Drug-Related Problems, namely drugs without indications at 14.29%, indications that are not treated by 59.52%, inappropriate drug selection by 16.47 %, excess doses by 0%, under doses by 2.38%, side effect reactions are 0%, drug interactions are 7.14%, and failure to receive drugs is 0%.

ACKNOWLEDGMENT

The author would like to thank RSUP Dr. M. Djamil Padang for allowing and providing facilities for this ongoing research. This research was entirely funded personally by the authors. All authors state that there is no potential conflict of interest with the research, authorship, and publication of this article.

REFERENCES

- [1]. American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Heart disease and stroke statistics update: a report from the American Heart Association*. Circulation; 2016.
- [2]. Kementerian Kesehatan RI. Info DATIN Situasi Kesehatan Jantung. Jakarta. *Pusat data dan Informasi Kementerian Kesehatan RI*. Jakarta; 2014.
- [3]. Scottish Intercollegiate Guidelines Network. *Management of Patients with Stroke*. A National Clinical Guidelines Recommended for Use in Scotland; 2009
- [4]. Milikan C.H, Dowell F, Easton J.D. *Stroke*. 2nd ed. Lea & Febiger. Philadelphia. 2011; 33-62.
- [5]. Martono H. and Kuswardani R. A. T. *Ilmu Penyakit Dalam*. Jakarta Pusat: Interna Publishing; 2009.
- [6]. Kishore, A.K, Vail, A., Chamorro, A., Garau, J., Hopkins., S.J., Napoli, M., et al. *How Is Pneumonia Diagnosed in Clinical Stroke Research? A systematic Review and Meta Analysis*, *Stroke*. 2015; 46 (5). 1202 – 1209.
- [7]. Sui, R and Zang L. Risk Factors of Stroke – Associated Pneumonia in Chinese Patients, *Neurological Research*. 2011; 33 (5). 508 – 513.
- [8]. Perhimpunan Dokter Spesialis Saraf Indonesia. *Guideline Stroke*. PERDOSSI. Penerbit Jakarta; 2011.
- [9]. Fagan, S. C., and Hess, D. C. *Cardiovaskular ; Stroke In DiPiro J.T., et al, Pharmacotherapy: 10th Edition*, The McGraw-Hill Companies. United States of America; 2017.
- [10]. Presley B. Terapi Penatalaksanaan Farmakologi Stroke Iskemik Akut Terapi, *Rasional*. 2014; 12(1). 6–8.
- [11]. Priyanto. *Farmakoterapi dan Teknologi Medis*, Lembaga Medis dan Konsultasi Farmakologi, Jawa Barat; 2009.
- [12]. Kishore, A.K, Vail, A., Chamorro, A., Garau, J., Hopkins., S.J., Napoli, M., et al. *How Is Pneumonia Diagnosed in Clinical Stroke Research? A systematic Review and Meta Analysis*, *Stroke*. 2015; 46 (5). 1202 – 1209.
- [13]. Khalillullah, S. A.. *Penggunaan Antiplatelet (Aspirin) pada Akut Stroke Iskemik*, Medicin University of Syiah Kuala; 2011.
- [14]. Lacy, C.F., Amstrong, L.L., Goldman, M.P., & Lance, L.L. *Drug Information Handbook*. 17 th edition, Lexi – Comp Inc, Ohio; 2009.
- [15]. Departemen Kesehatan RI. Kategori Usia. 2009 [di unduh 12 Februari 2019]; Tersedia dari <http://kategori-umurmenurut-Depkes.html>.