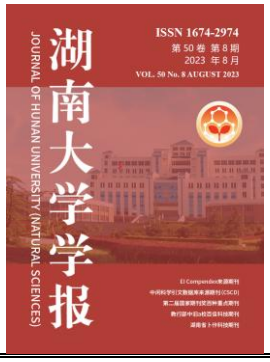

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Potential Drug-Related Problems in Ischemic Stroke Patients and Their Effect on Clinical Outcomes at RS X, East Jakarta, in 2019

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Abstract: Background, Stroke is a circulatory disorder of the brain caused by narrowing of blood vessels due to comorbidities such as hypertension and hyperlipidemia. Thus, causing functional disorders of the brain in the form of neurological deficits/nerve paralysis for 24 hours or more. Treatment of stroke with comorbidities will result in Drug Related Problem (DRP). The purpose of this study was to determine DRPs and their effects on clinical outcomes in ischemic stroke patients at RS X East Jakarta in 2019. Methodology, This study uses a cross-sectional design, and data collection was carried out retrospectively on 120 medical records of ischemic stroke patients in 2018. The data obtained were analyzed with SPSS, for drug interactions based on literature and observations of prescriptions for ischemic stroke patients, The results of the study found 36.07% drug interactions, 29.51% indications without drugs, 9.29% drugs without indications, 6.56% frequency of administration exceeding the rules of use, 5.46% doses too high, 4.37% frequency of administration less than the rules of use, 2.73% doses too low, 2.19% too many drugs for the same indications, 1.64% of each drug did not comply with treatment guidelines, inappropriate drugs due to contraindications, and 0.55% inappropriate duplication of active substance. There was an association between DRP and patient clinical outcomes but not significant. Recommendation, Better collaboration among doctors, pharmacists, and other health workers is needed to obtain safe and effective treatment outcomes.

Keywords: clinical outcome, drug-related problem, ischemic stroke.

2019年雅加达东部 RS X医院缺血性中风患者的潜在药物相关问题及其对临床结果的影响

摘要：背景，中风是由于合并症如高血压和高脂血症引起的血管变窄而引起的脑循环障碍。因此，以神经缺陷/神经麻痹的形式引起脑的功能障碍24小时或更长时间。中风与合并症的治疗将导致药物相关的问题。本研究的目的是确定药物相关问题及其对2019年雅加达RS X东区缺血性卒中患者临床结果的影响。方法，本研究采用横断面设计，对2018年缺血性卒中患者的120份病历进行了回顾性数据收集。根据文献和缺血性脑卒中患者处方的观察，研究结果发现36.07%的药物相互作用，29.51%的适应症，9.29%的药物没有适应症，6.56%的给药频率超过使用规则，5.46%的剂量过高，4.37%的给药频率低于使用规则，2.73%的剂量

过低，2.19%的药物过多。每种药物的1.64％不符合治疗指南,不适当的药物由于禁忌症,和0.55%不适当的重复活性物质.药物相关问题与患者临床结果之间存在关联，但不显着。建议，医生，药剂师和其他卫生工作者之间需要更好的合作，以获得安全有效的治疗结果.

关键词：临床结果、药物相关问题、缺血性中风.

1. Introduction

Stroke is also known as cerebral circulatory disorder (GPDO), which results in functional brain disorders in the form of neurological deficits or paralysis [1]. Based on WHO data from 2016, stroke is the second leading cause of death in the world after ischemic heart disease [2]. The South East Asian Medical Information Centre (SEAMIC) reported that the largest stroke death rate occurred in Indonesia, followed by the Philippines, Singapore, Brunei, Malaysia, and Thailand.

Stroke is divided into two types: ischemic stroke and hemorrhagic stroke. In Indonesia, ischemic stroke is the most common type (52.9%), followed by intracerebral hemorrhage (38.5%), embolism (7.2%), and subarachnoid hemorrhage [3]. Some research results have shown the existence of drug-related problems (DRP) that occur for treating ischemic stroke patients.

DRP are unwanted events that occur in patients associated with drug therapy that have the potential to interfere with the expected success of healing. DRP categories include untreated indications, drugs with inappropriate indications, incorrect drugs, drug interactions, overdoses, subtherapeutic doses, unwanted drug reactions, and failure to receive drugs [4].

Research in Indonesia conducted by [5] regarding the identification of potential DRPs in non-hemorrhagic stroke patients showed that the most common DRP categories were indications without drugs (62.26%), followed by drug interactions (58.49%), too low doses (41.51%), too high doses and improper drug selection (24.53%), and the rest of the drug without indication. Research conducted in India by Celin et al. [6] related to DRP in stroke patients actually shows that the most common problem is drug interactions (25%), followed by the use of drugs without indication (15%), and the rest are unwanted drug reactions [6].

Previous studies have shown that drug-related problems still often occur for treating patients with ischemic stroke. The occurrence of DRPs can hinder the achievement of therapeutic goals. Errors in prescribing medications can lead to negative outcomes for health, pose significant challenges to health care, and contribute to morbidity and quality of life in patients [7].

Based on previous research, this study will study DRPs that occur in ischemic stroke patients and their effects on patient clinical outcomes in the inpatient installation of RS X East Jakarta in 2019 considering that this research has never been conducted before.

2. Research Methodology

The research was conducted at RS X, East Jakarta 2019. This study used a *cross-sectional* design and the variable data collected in this study were retrospectively obtained from patient medical records.

The population in this study was all ischemic stroke patients hospitalized at RS X in 2019 East Jakarta, totaling 243 patients. The sample in this study was a population that met the inclusion criteria, which was 120 patients. The sampling technique used was total sampling, i.e., all patients who met the criteria were taken as research samples.

The inclusion criteria in this study were as follows: 1) patients undergoing ischemic stroke therapy with or without other comorbidities at RS X East Jakarta in 2019; 2) patients with complete medical records and patient status (patient name, gender, age, primary diagnosis, complications, date of treatment, indications for treatment and drugs used; 3) patients aged 18 years.

The exclusion criteria in this study were: 1) pregnant and lactating women; 2) the patient dies; 3) the patient is forcibly discharged before therapy is completed.

Data collection through recording medical records of ischemic stroke patients at RS X, East Jakarta, Year 2019 that meet the inclusion criteria include: 1) patient identity (name, gender, age); 2) disease diagnosis, patient's disease history, and patient complaints; 3) use of the drug (type, dosage regimen, and rules of use); 4) laboratory result data; 5) patient clinical outcomes (neurological function and blood pressure). The collected data are then analyzed so that conclusions are obtained from the study.

The parameters measured in ischemic stroke are neurological function and blood pressure in post-treatment patients. The patient's neurological function was measured (Table 1) using the Glasgow Coma Scale [8], and the patient's blood pressure was measured using a sphygmomanometer by medical personnel. Both clinical parameters can be observed from the patient's medical record. Study flowchart is shown in Fig. 1.

Table 1 The Glasgow Coma Scale (GCS) category scores

Category GCS	Scores
Compos mentis	15–14
Apathy	13–12
Delirium	11–10
Somnolen	9–7
Drowsiness	6–5
Semi coma	4
Comma	3

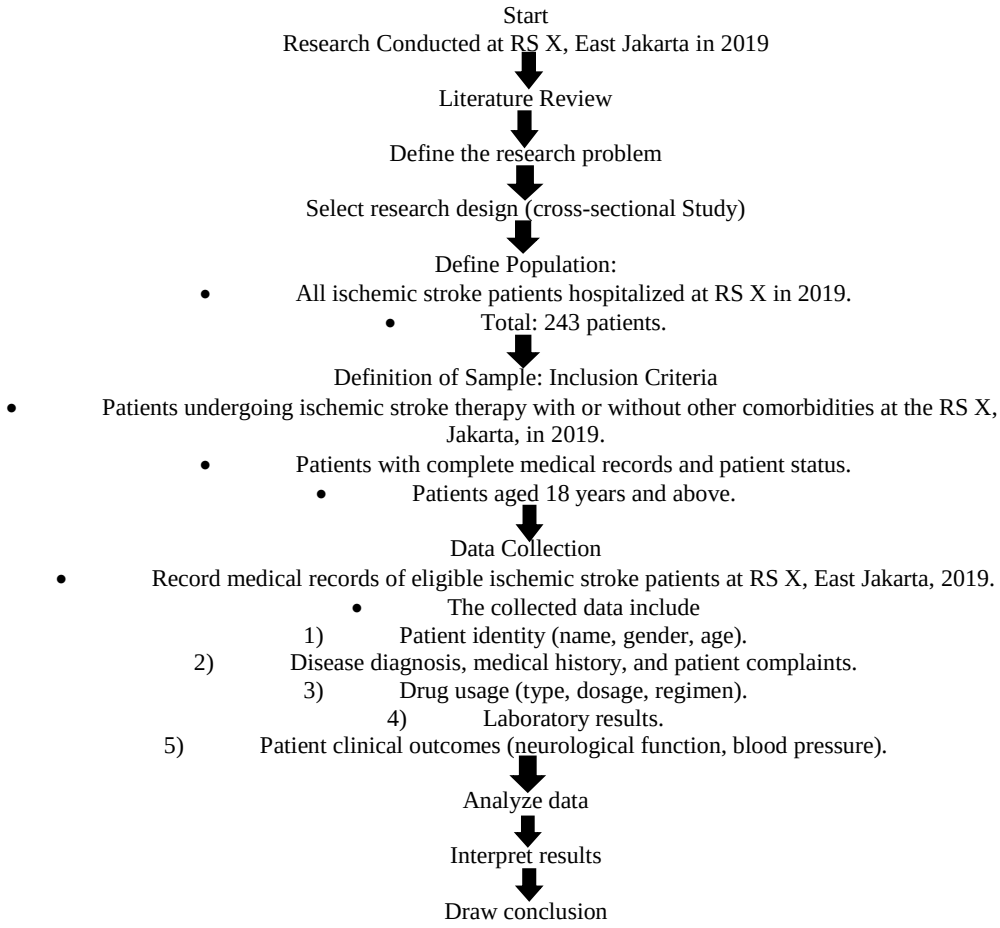

Fig. 1 Flowchart of the research methodology (Developed by the authors)

On the basis of JNC 8, the patient's blood pressure is declared controlled if it meets the following criteria [9] (Fig. 2):

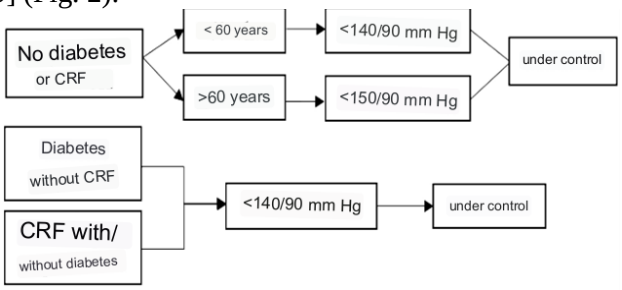

Fig. 2 Blood pressure outcome categories with age (Developed by the authors)

3. Results

3.1. Patient Characteristics

Based on 120 samples collected, 53.3% of them were male patients and 46.7% were female patients. The age of most patients ranges from 46 to 65 years, the majority of patients are given therapy ≥ 5 drugs (polypharmacy), when attacked by stroke, the majority of patients suffer from high blood pressure ≥160/100 mmHg with *a Glasgow Coma Scale* (GCS) *compos mentis* score, and most patients (93.3%) have comorbidities. The most common comorbidities are hypertension, followed by dyslipidemia, diabetes mellitus, and hypokalemia.

3.2. Drug Use Profile

Table 2 shows that citicholine is the most commonly administered ischemic stroke drug, followed by many ischemic stroke drugs from the antiplatelet group, namely clopidogrel and aspirin. In addition to ischemic stroke drugs, patients are administered drugs to overcome comorbidities.

Table 2 Distribution of ischemic stroke drug use among inpatient ischemic stroke patients at RS X, East Jakarta, 2019 (Developed by the authors)

Medicine		Frequency of Use
Ischemic Stroke Medication		
Antiplatelet		
-	Klopidogrel	56
-	Aspirin	39
-	Cilostazol	6

Continuation of Table 2		
Anticoagulants		
-	Warfarin	8
-	Rivaroksaban	1
Vitamins / supplements		
-	Sitikolin	117
Neurotropik		
-	Pirasetam	13

Comorbidities that are most often given to patients are drugs to treat hypertension and hyperlipidemia. The most commonly administered antihypertensive drugs are amlodipine followed by valsartan and bisoprolol. The drug to treat hyperlipidemia that is most often given is atorvastatin.

3.3. Drug Related Problems

Table 3 above shows the types of DRPs that occurred in patients with ischemic stroke at the 2019 RS X inpatient installation in East Jakarta. There were 175 cases of DRPs analyzed.

Table 3 Distribution of DRP category in inpatient ischemic stroke patients at RS X in 2019, where JP - number of the patients (Developed by the authors)

DRP Category	JP (n = 120)	Percentage (%)	Frequency (n = 175)	Percentage (%)
Drug selection				
Medication not according to the treatment guidelines	3	2,5	3	1,71
Inappropriate drug due to contraindications	3	2,5	3	1,71
Drugs without indications	12	10	12	6,86
Indications without drugs	46	38,33	52	29,71
Drug Interactions	49	40,83	64	36,57
Improper duplication of the active substance	1	0,83	1	0,57
Too much medication for the same indications	4	3,33	4	2,29
Dosage selection				
Too low a dose	5	4,17	5	2,86
Too high a dose	10	8,33	10	5,71
The frequency of administration is less than the rule of use	8	6,67	8	4,57
Frequency of administration exceeds the rules of use	13	10,83	13	7,43
Improper timing of drug administration instructions	0	0	0	0

In the drug selection category, the DRPs that occurred the most were drug interactions (36.57%), followed by indications without drugs (29.71%), drugs without indications (6.86%), too many drugs for the same indications (2.29%), drugs not according to treatment guidelines, and inappropriate drugs due to contraindications (1.71% each). The DRP category of drug selection that occurred the least was improper duplication of active substances (0.57%).

The frequency of administration exceeding the rules of use (7.43%) was the DRP of the most common dose selection category followed by too high a dose (5.71%), a frequency of administration less than the rules of use (4.57%), too low a dose (2.86%), and improper drug administration time instructions (0%).

3.4. Clinic Outcome

Table 4 shows that the majority of patients go home with their blood pressure under control, and the rest go home under control.

Table 4 Distribution of blood pressure clinical outcomes (Developed by the authors)

Blood Pressure	Frequency (n = 120)
Controlled	71
Uncontrollable	49
Total	120

Table 5 shows that all patients with ischemic stroke who were hospitalized at Budhi Asih Hospital in 2018 returned home in a state of *compos mentis* consciousness.

Table 5 Distribution of the clinical outcomes of neurological function (Developed by the authors)

Neurological Functions	Frequency (n = 120)
Reached	120
Not reached	0
Total	120

3.5. Bivariate Analysis

Table 6 shows that the relationship between DRPs and clinical blood pressure outcomes using Chi-square analysis obtained P = 0.138 (P > 0.05), so it was concluded that there was no significant relationship between drug-related problems and clinical outcomes of patients' blood pressure.

Table 6 Analysis of the effect of DRPs on the clinical outcomes of blood pressure (Developed by the authors)

Event DRPs	Blood Pressure Clinic Outcomes				P Value
	Controlled		Uncontrollable		
	Sum	% of total controlled blood pressure	Sum	% of total uncontrolled blood pressure	
Ada	57	55,9%	45	44,1%	0,138
Tidak ada	14	77,8%	4	22,2%	
Total	71	59,2%	49	40,8%	

4. Discussion

The majority of patients in this study were male. The results of this study are in accordance with research conducted by the American Heart Association and at RSUP Prof. Dr. R. D. Kandou, who stated that the prevalence of ischemic stroke patients is more male than female [10, 11]. The incidence of stroke is experienced by many men, because men have the hormone testosterone which can increase blood levels *of low density lipoprotein* (LDL). High LDL levels can cause cholesterol levels in the blood to increase, so the risk of degenerative diseases also increases [12, 13].

Most patients aged over 40 years to the elderly are more susceptible to stroke. Research conducted in Surabaya in 2017 showed that as many as 75% of stroke patients were aged over 55 years [14]. Ischemic stroke tends to occur in older age groups because of impaired blood flow. Blood vessels in older people tend to undergo degenerative changes and begin to show the results and processes of atherosclerosis [15].

The majority of patients suffer from hypertension during ischemic stroke, especially in the class of grade II hypertension (≥ 160/100 mmHg). Research conducted in Surabaya in 2017 also showed 97.7% of patients suffered from hypertension when they had stroke [14]. Hypertension is a major risk factor for ischemic stroke, with high systolic and systolic pressure. The higher a person's blood pressure, the greater the risk of stroke [16]. Hypertension can thin the walls of blood vessels and damage the inside of blood vessels, which encourages the formation of atherosclerotic plaques, making it easier for brain blockage or hemorrhage to occur [17].

In this study, it is known that the Glasgow Coma Scale (GCS) shows that the majority of patients after ischemic stroke are *compos mentis.* GCS scores are an accurate predictor of mortality in ischemic and hemorrhagic stroke patients. GCS assesses patients based on their level of consciousness. GCS scores had an accuracy of 88% in predicting patient mortality [18].

In this study, the grouping of the number of drugs given was divided into 2 categories, namely, not polypharmacy (< 5 drugs) and polypharmacy (≥ 5 drugs) [19]. The results showed that most of the patients belonged to the category of polypharmacy. Research conducted by Isra et al. [20] also showed the existence of polypharmacy in stroke therapy with an average use of drugs by patients of more than 10 drugs. The administration of other drugs is intended to overcome possible side effects and comorbidities; therefore, patients need combination therapy with varying amounts of drugs.

The results of the study showed that most patients belong to the category of polypharmacy. The grouping of the number of drugs given is divided into 2 categories, namely, not polypharmacy (< 5 drugs) and polypharmacy (≥ 5 drugs) [19]. [20] also showed the existence of polypharmacy in stroke therapy with an average use of drugs by patients as many as more than 10 drugs. The administration of other drugs is intended to overcome possible side effects and comorbidities; therefore, patients need combination therapy with varying amounts of drugs.

In addition to suffering an ischemic stroke, most patients in the study suffered from other comorbidities. In this study, the most common comorbidities experienced by inpatient ischemic stroke patients at Budhi Asih Hospital 2018 were hypertension, followed by dyslipidemia, diabetes mellitus and hypokalemia. The results of this study are also similar to research conducted in Yogyakarta in 2017, where the most common comorbidities suffered by stroke patients are hypertension, followed by dyslipidemia, atrial fibrillation and diabetes mellitus [21].

The occurrence of increased blood pressure is a compensatory mechanism for the body to meet the needs of blood supply that is less due to lesions [22]. People with hypertension have 5.48 times the risk of stroke compared with those without hypertension. The next comorbidity is dyslipidemia. Abnormal serum lipid conditions and hypercholesterolemia have a major effect on the formation of atherosclerosis and plaque [23]. Cerebral atherosclerosis is the most common cause of ischemic stroke [24]. Comorbidities that are also widely experienced include diabetes mellitus. Blood sugar levels often increase at the beginning of a stroke as a reaction to compensatory mechanisms or as a result of stress mechanisms. High blood sugar can worsen brain damage; therefore, it is necessary to reduce blood sugar levels [14]. Hypokalemia is the next comorbidity. Post-stroke hypokalemia is common and can be associated with a poor prognosis [25]. Research conducted in Bangladesh in 2012 showed that as many as 31% of acute stroke patients experienced impaired potassium levels 26.

Drugs not according to treatment guidelines occur in patients with blood pressure of 180/100mm Hg, but only amlodipine therapy is administered. According to JNC 8, blood pressure >160/100 mmHg belongs to the category of hypertension grade 2 [9]. The patient did not suffer from diabetes mellitus or chronic kidney failure; therefore, the blood pressure target achieved was below 140/90 mmHg. Therapy for grade 2 hypertension without compelling indication is a combination of 2 antihypertensive drugs class ACEI (Angiotensin-converting enzyme inhibitors) or ARBs (Angiotensin II receptor blockers) with thiazide diuretics or CCB (Calcium channel blockers) [9]. This DRP is also in patients administered warfarin to treat ischemic stroke. Aspirin 50–335 mg daily is more recommended than warfarin because it is considered more effective in preventing recurrent stroke [27].

The drug is inappropriate because contraindications occur in the administration of aspirin where laboratory results show indications of leukocytosis, and aspirin administration can increase leukocyte levels. In addition, aspirin is also given to patients who also have indications of hypertension, this is not appropriate because one of the side effects of NSAIDs is increasing blood pressure [28].

The drug without indication occurs with the administration of metformin and glimepiride. Improper use of glimepiride can cause hypoglycemia [29]. The drug without subsequent indications was found by the administration of potassium chloride. Potassium chloride supplements are used to treat or prevent hypokalemia. Administration of potassium chloride without indication can cause an excessive increase in potassium levels (hyperkalemia). High potassium levels can also cause serious complications, particularly in people with kidney failure [30]. Drugs without subsequent indications include atorvastatin and simvastatin. The use of atorvastatin and simvastatin without indication can increase the risk of liver damage up to an increase in blood sugar levels [31]. The next drug without indication is allopurinol, the patient's laboratory results show normal uric acid levels. The drug without the last indication is ceftriaxone. The unnecessary use of antibiotics leads to the development of resistance to certain bacteria [32].

Indications without drugs are found in patients with indications of dyslipidemia. Lipid-lowering therapy in patients with high cardiovascular risk decreases the incidence of stroke and TIA [33]. The next indication without medication is hyperuricemia. Uric acid because of purine synthesis in hyperuricemia is a risk factor for stroke other than hypertension and diabetes mellitus (DM) [34]. The next indication without medication is hypokalemia. Hypokalemia is a serious condition that is often involved in various cardiovascular diseases. In the research of Macdonald and Allan [35], it was found that high blood potassium levels inhibit platelet aggregation, so ischemic stroke can be prevented[35]. The next indication without medication is hyperglycemia. People with diabetes have a greater risk of ischemic stroke than people without a history of DM because it can trigger atherosclerosis faster than people who do not suffer from DM. Hypertension is an indication without subsequent drugs that occurs in patients with ischemic stroke. Hypertension is a major risk factor for ischemic stroke. Systolic blood pressure should be managed to achieve the target of <140 mmHg and diastolic blood pressure <90 mmHg, for patients without a history of diabetes mellitus and chronic renal failure aged ≥ 60 years, then the systolic blood pressure target is < 150 mmHg and diastolic blood pressure < 90 mmHg 19. The next occurrence of DRPs indicative without drugs is leukocytosis. A high leukocyte count is an inflammatory reaction that secretes proinflammatory cytokines IL-1 and TNF α. Leukocytes will worsen neurological deficits by increasing the number of leukocytes which will result in excess production of free radicals and toxic substances [36]. Leukocytes can also cause occlusion in the cerebral circulation [37].

In this study, there was an incidence of improper duplication of active substances, where two drugs with the same therapeutic group were given simultaneously, namely in joint administration of BK III and ambroxol. BK III is a sputum-thinning drug produced by RS X in East Jakarta, which contains ambroxol, chlorpheniramine maleate, bromheksin, salbutamol, and guaifenesin. Patients are also given ambroxol tablets. Duplication of this active substance can lead to unexpected overdose, thereby increasing the risk of side effects [38].

The category of too many drugs for the same indication occurs in the joint administration of warfarin and aspirin, and aspirin and clopidogrel. Klopidogrel and aspirin are ischemic stroke drugs of the antiplatelet group, whereas warfarin is an anticoagulant group. The European Society of Cardiology (ESC) guidelines state that the addition of aspirin to oral anticoagulants does not reduce the risk of stroke or vascular events (including myocardial infarction) but substantially increases the incidence of bleeding [39]. Combination therapy with aspirin and clopidogrel was no more effective than the use of a single aspirin in reducing the incidence of stroke, myocardial infarction, or death due to cardiovascular disease [40].

Improper drug combinations are defined as the presence of possible or potential drug interactions in a patient. Drug interactions based on their mechanisms are divided into three categories: pharmacokinetic, pharmacodynamic, and unknown. In this study, the majority of patients experienced pharmacodynamic drug interactions, which means that the drugs given interact with each other in the same receptor system, workplace, or physiological system so that additive, synergistic, and antagonistic effects occur. Next is pharmacokinetic drug interactions. This indicates that one of the drugs affects the absorption, distribution, metabolism, or excretion of the second drug so that the plasma levels of both drugs will increase or decrease because of increased toxicity or decreased effectiveness of the drug [41]. The last drug interaction is not clearly known whether it is included in the pharmacodynamic or pharmacokinetic mechanism. Some alternatives to managing drug interactions include avoiding combinations by choosing non-interacting replacement drugs, adjusting drug doses, monitoring patients, or continuing treatment as before if the combination of interacting drugs is the optimal treatment or if the drugs are not clinically meaningful.

Drug interactions based on severity are divided into three categories: severe (major), moderate (moderate),

and mild (minor). In this study, the most severity-based drug interactions were moderate followed by major and minor drug interactions. In addition, drug iterations are divided into two categories: beneficial drug interactions and adverse drug interactions.

Moderate drug interactions include the type of drug interaction that is preferred to be prevented and overcome if the resulting drug interaction is more harmful than the benefits. The majority of moderately beneficial drug interactions occur with the administration of amlodipine with bisoprolol. The results of research by Gottwald-Hostalek U et al. [42] showed that the combination of amlodipine and bisoprolol showed better effectiveness than monotherapy and good tolerability, making this combination a useful alternative for second-line treatment. Moderate adverse drug interactions are most prevalent with aspirin and valsartan. NSAIDs (aspirin) decrease renal prostaglandin synthesis, thereby affecting fluid homeostasis and may reduce the antihypertensive effect (valsartan) [43].

Next is a major drug interaction that is prioritized to be prevented and overcome because it can cause life-threatening effects or permanent damage. Major interacting drugs include valsartan with spironolactone, candesartan with spironolactone, potassium chloride with candesartan, potassium chloride with telmisartan, and potassium chloride with spironolactone. Each of these drug uses simultaneously can give rise to hyperkalemia, in severe cases, it can lead to kidney failure, muscle paralysis, irregular heart rhythms, and cardiac arrest [44]. Another major drug interaction was found in the use of the drug omeprazole with clopidogrel. The use of both together can reduce the effectiveness of clopidogrel in preventing heart attack or stroke, thus increasing cardiovascular events [45].

Minor drug interactions are those that may be disruptive or unwittingly occurring. In this study, no minor drug interactions were observed in patients.

An excessively low-dose DRP is defined as a dose given to a patient lower than the minimum dose based on the literature. Too low a dose occurs with the administration of cilostazol, gabapentin, and metformin. Cilostazol at a dose of 2x50 mg, to treat ischemic stroke should be 2x100 mg [43]. Gabapentin at a dose of 2x100 mg, as an anticonvulsant, should be 300 mg on the first day, 2x300 mg on the second day, 3x300 mg on the third day [46]. Metformin at a dose of 2x250 mg, for hyperglycemia should be 2x500 mg or 1x850 mg orally [46].

An overdose is defined as a dose given to a patient that is greater than the maximum dose that can be administered based on the literature. In this study, it was found that the incidence of too high doses in the administration of phenodibrate, amlodipine, and famotidine was high. Phenofibrate at a dose of 1x300 mg while the maximum dose of phenobrate per day is 200 mg. Famotidine as much as 3x2 tablets, the dose per tablet is 20 mg, while the maximum dose of fatomidine per day to treat peptic ulcers is 1x40 mg or 2x20 mg for 4-8 weeks. Amlodipine at a dose of 1x15 mg, while the maximum dose of amlodipine per day is 10 mg [47].

The frequency of administration less than the rules of use occurs in the administration of gabapentin, phenytoin, nitroglycerin, and metformin. Gabapentin is administered with a frequency of 2x100 mg, to treat peripheral neuropathic should be 3x100 mg. Phenytoin with a frequency of 2x100 mg, as an anti-convulsant should be 3x100 mg. Nitroglycerin with a frequency of 1x2.5 mg, to treat angina should be 3-4 x 2.5-6.5 mg with a maximum dose of 26 mg/day [47]. Metformin with a frequency of 1x500 mg, to overcome hyperglycemia should be given 2x500 mg [28].

The frequency of administration exceeding the rules of use occurs in the administration of allopurinol, omeprazole, and hydroxyurea. Allopurinol is given with a frequency of 3x100 mg, while as uric acid maintenance therapy should be 1x200-300 mg (single dose). Omeprazole with a frequency of 2x40 mg, as peptic ulcer therapy should be 1x40 mg. Hydroxyurea is given to treat leukemia as a single dose at a dose of 20–30 mg/kg body weight, but patients are given hydroxyurea frequency of 3x1. The frequency of drug administration that exceeds the rules of use can result in drug levels in the blood exceeding the maximum level of drugs in the blood, causing unexpected effects such as side effects or toxicity [43].

Improper drug administration time instructions are defined as drug administration times that do not comply with the literature. In this study, there was no occurrence of DRPs, and the instructions for the timing of drug administration were incorrect. In addition to the dosage, the method, time, and duration of drug administration must also be appropriate. If one of the four conditions is not met, the therapeutic effect is not achieved [48].

Clinical outcomes showed that most patients returned home with their blood pressure under control (59.2%), and the rest returned home with their blood pressure out of control (40.8%). The treatment of hypertension in ischemic stroke patients needs to be improved again because there are still patients who go home with high blood pressure. This can be caused by DRP that occurs causing the expected blood pressure outcome not to be achieved, but a drastic decrease in blood pressure is also not recommended. Long-term blood pressure should be low but not be lowered acutely as it can lead to watershed infarction. The limit of lowering blood pressure as much as possible to 20-25% [26].

The clinical outcome of neurological function can be seen from the patient's level of awareness and improvement of symptoms experienced through

improvement of motor function using the Glasgow Coma Scale (GCS) method. In this study, all ischemic stroke patients who were hospitalized at Budhi Asih Hospital returned home with GCS compos mentis. Compos mentis is a fully conscious condition in which the patient has a very good attitude toward himself and the environment [8,49].

Based on the results of bivariate analysis between the incidence of DRPs on the patient's blood pressure clinical outcomes, it is known that the P value (significance) obtained is 0.138. A P value of > 0.05 indicates that there is an association, but not significant, between drug-related problems and clinical outcomes of patients' blood pressure.

5. Conclusion

The study found a relationship between DRPs effects on clinical outcomes in ischemic stroke patients at RS X East Jakarta in 2019, but it was insignificant. The findings also revealed that the types of DRPs that occur most in ischemic stroke patients in the inpatient installation of RS X East Jakarta 2019 are drug interactions, indications without drugs, drugs without representations, frequency of administration exceeding the rules of use, doses too high, frequency of administration less than the rules of use, too many medications for the same indications, doses too low, drugs not according to treatment guidelines, improper medication due to contraindications, and improper duplication of the active substance. There was an association between the incidence of DRPs and clinical outcomes of patients' blood pressure, but it was insignificant. All patients in the study returned home with excellent neurological function and level of consciousness (compos mentis). These findings are original and contribute to the literature on the impact of clinical outcomes in patients with ischemic stroke for improving better services. The study has certain limitations that need to be acknowledged. First, most patients in the study were male, in alignment with prior research; however, this gender bias could limit the generalizability of the findings. Additionally, the single-center nature of the study, focusing on a single hospital, might restrict the representation of diverse patient populations and healthcare settings, thereby affecting the broader applicability of the results. Finally, the use of retrospective patient medical records, while valuable for data collection, could introduce concerns regarding the accuracy and completeness of the data, warranting careful consideration in the interpretation of the findings. This study offers insights into factors affecting the treatment and outcomes of ischemic stroke patients.

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