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Evaluation of drug use in stroke patients at the inpatient unit of Brebes Hospital, Central Java

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ABSTRACT

Background: Effective stroke treatment is complicated by factors such as polypharmacy, drug interactions, and side effects, leading to drug-related problems (DRPs) that hinder therapeutic outcomes. Evaluating drug use in stroke patients is crucial to ensure rational, safe, effective, and efficient treatment, ultimately improving therapeutic outcomes.

Objective: This study aimed to evaluate the drug use patterns in inpatient stroke patients at Brebes Hospital, focusing on the appropriateness of drug selection, dosage, administration, and the impact of patient characteristics on DRPs.

Method: A retrospective, descriptive evaluative design was employed, with data collected from medical records of stroke patients hospitalized at Brebes Hospital between May and July 2022. A total of 135 patients (110 ischemic, 25 hemorrhagic stroke) were included through consecutive sampling. Univariate analysis was used to describe patient characteristics and treatment patterns, while bivariate analysis with the chi-square test assessed the relationship between patient characteristics and DRPs.

Results: The most common medications included citicoline (88.15%), clopidogrel (68.85%), and amlodipine (40.48%). DRPs were identified, including non-compliance with guidelines (1 case), contraindicated drugs (5 cases), and inappropriate drug selection (1 case). Notably, five cases of contraindicated use of omeprazole with clopidogrel and one case of phenytoin without indication were observed. Patient characteristics such as age and comorbidities did not significantly influence the incidence of DRPs ($p > 0.05$).

Conclusion: The study found irrational drug use in stroke patients, with DRPs posing challenges for treatment optimization. Addressing DRPs through improved prescribing practices and pharmacist intervention is crucial to enhancing therapeutic outcomes in stroke management.

Keywords: stroke, drug-related problems (DRPs), rational drug use, pharmacotherapy, drug use evaluation

Introduction

Stroke is a sudden, non-traumatic disruption of cerebral blood flow that can progress rapidly. In Indonesia, particularly in Central Java, the prevalence of stroke has been increasing each year and remains one of the leading causes of death [1]. Treating stroke patients is complex and often involves challenges such as dose inaccuracies, polypharmacy, drug interactions, and adverse side effects, which can arise from various risk factors or comorbidities. These issues frequently result in irrational treatment practices, preventing the desired therapeutic outcomes [2].

Evaluating drug use in stroke patients is crucial to ensuring rational and effective treatment. This evaluation is a continuous clinical pharmacy service that provides insights into drug use patterns in hospitals and aims to optimize treatment for safety, efficacy, and efficiency [3]. Therefore, the purpose of this study is to analyze the treatment patterns and evaluate drug use in

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Table 1. Characteristics of stroke patients in the inpatient department of Brebes Hospital, May-July 2022

Patient characteristic		Number	Percentage (%)
Age	< 60 years	67	49.63
	≥ 60 years	68	50.37
Sex	Female	73	54.08
	Male	62	45.92
Comorbidities	Low	19	14.07
	Medium	39	28.89
	High	77	57.04
Length of stay	≤5 days	110	81.48
	>5 days	25	18.52

inpatient stroke patients at Brebes Hospital. This includes assessing the appropriateness of drug selection, dosage forms, dose accuracy, treatment duration, dispensing practices, drug administration, patient behavior, and identifying any other relevant issues.

Methods

This study employed a retrospective descriptive evaluative design conducted from May 2022 to July 2022. Ethical approval for the research was granted by the Health Research Ethics Committee of Muhammadiyah Purwokerto University, with registration number KEPK/UMP/12/II/2023.

Population and sample

The study population consisted of stroke patients admitted to Brebes Hospital between May 2022 and July 2022. A total of 135 patients were included in the sample, comprising 110 ischemic stroke patients and 25 hemorrhagic stroke patients. The inclusion criteria were patients aged over 18 years with a confirmed diagnosis of stroke. Exclusion criteria included incomplete medical records and patients who died during treatment. Samples were selected using consecutive sampling. Data were collected from patients' medical records, which included patient demographics, time of stroke onset, hospital arrival time, initial diagnosis, treatment plan, medication profile, laboratory results, and any additional examinations.

Instruments

Data were collected using data collection sheets and drug use evaluation forms, based on the Pharmaceutical Care Network Europe (PCNE) V8.02 classification. Relevant guidelines and literature were used, including the Decree of the Minister of Health of the Republic of Indonesia Number HK.01.07/Menkes/394/2019 concerning National Guidelines for Medical Services for Stroke Management, *Pharmacotherapy: A Pathophysiologic Approach* (11th Edition), the American Geriatrics Society 2015 Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults, and the KDIGO 2022 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease.

Analysis

Univariate analysis was conducted to describe patient characteristics, medication patterns, and the evaluation of drug use. Bivariate analysis using the chi-square test was performed to determine the relationship between patient characteristics and the incidence of drug-related problems (DRPs).

Results

Patient characteristics

The characteristics of stroke patients observed in this study included gender, age, comorbidities, and length of treatment. As shown in Table 1, the majority of patients were aged ⩾ 60 years, accounting for 50.37% of the cases, while those under 60 years represented 49.63%.

Treatment pattern

The treatment pattern is detailed in Table 2, which shows that the primary cerebral activator and vasodilator drug used at Brebes Hospital was citicoline, administered intravenously. The most common dosing regimen was 2 x 500 mg (88.15%), followed by 2 x 250 mg (10.37%) and 3 x 500 mg (1.48%).

Table 2. Treatment pattern of stroke patients in the inpatient department of Brebes Hospital, May-July 2022

Drug class	Drug name	Dose	Route of administration	Number	Percentage (%)
Cerebral activators and vasodilators	Citicoline	2 x 250 mg	IV	14	10.37
		2 x 500 mg		119	88.15
		3 x 500 mg		2	1.48
Nootropic and neurotrophic agent	Mecobalamin	2 x 500 mcg	IV	133	98.51
Antiplatelet agents	Cilostazol	2 x 100 mg	PO	15	11.11
	Clopidogrel	1 x 75 mg		42	31.11
	Aspirin	1 x 80 mg		3	2.22
	Aspirin +Clopidogrel	1 x 80 mg; 1 x 75 mg		1	0.74
Antifibrinolytics	Tranexamic acid	1 x 6 g	IV	11	8.15
Antihypertensives	Candesartan	1 x 4 mg	PO	9	6.67
	Amlodipine	1 x 10 mg		51	37.78
	Nicardipine	5 mg/ h	IV	38	28.15
	Captopril	2 x 50 mg	PO	1	0.74
	Furosemide	2 x 20 mg		4	2.96
	Amlodipin+Furosemide	1 x 10 mg; 2 x 20 mg	PO	3	2.22
	Amlodipine +Nicardipine	1 x 10 mg; 5 mg/ h	PO IV	6	4.44
	Amlodipine +Candesartan	1 x 10 mg; 1 x 4 mg	PO	5	3.70
	Nicardipine +Candesartan	5 mg/h; 1 x 4 mg	IV PO	2	1.48
	Nicardipine +Furosemide	5 mg/h; 1 x 10 mg	IV PO	1	0.74
	Nicardipine +Amlodipine + Candesartan	5 mg/h; 1 x 10 mg; 1x 4 mg	IV PO PO	6	4.44
Vasoconstrictor	Norepinephrine	4 mcg	IV	2	1.48
Antidiabetic agent	Novorapid	0,5 U	SC	20	14.82
Antiseizure medications	Diazepam	1 x 20 mg	IV	4	2.96
	Fenitoin	1 x 15 mg	IV	3	2.22
	Diazepam + Fenitoin	1 x 20 mg; 1 x 15 mg	IV	2	1.48
Gastrointestinal agents	Omeprazole	1 x 80 mg	IV	38	28.15
	Ranitidine	1 x 25 mg		23	17.04
	Omeprazole + Ranitidine	1 x 80 mg; 1 x 25 mg	IV	13	9.63
Fluids and electrolyte solutions	Clinimix	2 x 500 ml	IV	1	0.74
	Ringer's lactate	500 ml		116	85.93
	NaCl	500 ml		18	13.33

Table 3. Evaluation of stroke treatment in the inpatient department of Brebes Hospital, May-July 2022

	Primary domain	Cause	DRP occurrence		Note
			Yes	No	
Prescription	Drug selection	Inappropriate drug according to guidelines/ formulary	1	134	Administration of fluids
		Inappropriate drug (within guidelines but otherwise contraindicated)	5	130	Administration of gastrointestinal medication
		No indication for drug	1	134	Administration of anticonvulsants
		Inappropriate combination of drugs, or drugs and herbal medications, or drugs and dietary supplements	0	135	
		Inappropriate duplication of therapeutic group or active ingredient	0	135	
		No or incomplete drug treatment in spite of existing indication	0	135	
		Too many drugs prescribed for indication	0	135	
	Drug form	Inappropriate drug form	0	135	
	Dose selection	Drug dose too low	0	135	
		Drug dose too high	0	135	
		Dosage regimen not frequent enough	0	135	
		Dosage regimen too frequent	0	135	
		Dose timing instructions wrong, unclear or missing	0	135	
	Treatment duration	Duration of treatment too short	0	135	
		Duration of treatment too long	0	135	
Dispensing	Dispensing	Prescribed drug not available	0	135	
		Necessary information not provided	0	135	
		Wrong drug, strength or dosage advised	0	135	
		Wrong drug or strength dispensed	0	135	
Usage	Drug use process	Inappropriate timing of administration or dosing intervals	0	135	
		Drug under-administered	0	135	
		Drug over-administered	0	135	
		Drug not administered at all	0	135	
		Wrong drug administered	0	135	
		Drug administered via wrong route	0	135	
	Patient-related	Patient uses/takes less drug than prescribed or does not take the drug at all	0	135	
		Patient uses/takes more drug than prescribed	0	135	
		Patient abuses drug (unregulated overuse)	0	135	
		Patient uses unnecessary drug	0	135	
		Patient takes food that interacts	0	135	
		Patient stores drug inappropriately	0	135	
		Inappropriate timing or dosing intervals	0	135	
		Patient administers/uses the drug in a wrong way	0	135	
		Patient unable to use drug/form as directed	0	135	
	Other problem	No or inappropriate outcome monitoring	0	135	
		Other cause; specify	0	135	
		No obvious cause	0	135	

Table 4. Relationship between patient characteristics and the incidence of DRP in stroke patients at Brebes Hospital, May-July 2022

Patient characteristic		DRP occurrence		P-value
		Yes	No	
Age	< 60 years	2	62	0.305
	≥ 60 years	5	66	
Sex	Female	3	70	0.514
	Male	4	58	
Comorbidities	Low	1	18	0.666
	Medium	1	38	
	High	5	72	
Length of stay	≤5 days	5	105	0.482
	>5 days	2	23	

Incidence of drug-related problems (DRP)

Table 3 highlights cases of drug-related problems. There was one instance where a drug selection did not adhere to guidelines, involving the administration of clinimix solution (500 ml glucose and 500 ml amino acids), despite the recommendation to avoid glucose/dextrose in stroke patients unless treating hypoglycemia [8]. Additionally, five instances of contraindicated drug use were observed, including the use of omeprazole in patients aged ⩾ 65 years who were also prescribed clopidogrel, which can reduce antiplatelet efficacy [9]. One case involved the inappropriate selection of phenytoin, where prophylactic anticonvulsants were given to a patient with ischemic stroke without seizures—an approach that is not recommended for ischemic stroke or intracerebral hemorrhage unless seizures occur [8].

Effect of patient characteristics on the incidence of DRP

As shown in Table 4, patient characteristics such as age, gender, comorbidities, and length of treatment were not found to significantly influence the incidence of drug-related problems ($p > 0.05$). The p-values for each characteristic were 0.305 (age), 0.514 (gender), 0.666 (comorbidities), and 0.482 (length of treatment).

Discussion

The patient characteristics observed in this study align with findings from the 2018 Riskesdas report, which indicated a higher prevalence of stroke among individuals aged ⩾ 60 years in Central Java and Indonesia, compared to those under 60 years of age. Stroke occurrence in younger individuals is often attributed to unhealthy lifestyle factors such as smoking, lack of physical activity, alcohol consumption, and poor dietary habits, including insufficient intake of fruits and vegetables. In this study, more female patients (54.08%) experienced strokes compared to males (45.92%), consistent with the 2018 Riskesdas report, which found a higher stroke prevalence in women (1.19%) compared to men (1.17%) [1]. This may be due to estrogen's role in increasing high-density lipoprotein (HDL) levels, which helps prevent atherosclerosis—a major cause of stroke [2].

The results also showed that the majority of patients had high comorbidities, with 57.04% having a Charlson Comorbidity Index (CCI) score greater than 1. Common comorbidities included diabetes mellitus and epilepsy. The majority of patients (81.48%) had a treatment duration of five days or less, indicating that medical complications during the treatment period can influence both clinical outcomes and the length of hospitalization [4].

In terms of treatment patterns, citicoline was the most commonly used cerebral activator and vasodilator at Brebes Hospital, administered intravenously. Citicoline supports brain function and helps repair cell membranes, particularly by enhancing phosphatidylcholine production, which is crucial for maintaining cell integrity in the brain [5, 6]. Additionally, mecobalamin, a nootropic and neurotrophic drug, was frequently used to improve brain function and inhibit homocysteine levels, which are predictors of recurrent stroke [6, 7].

Clopidogrel was the most widely used antiplatelet drug (68.85%), effective in preventing further ischemic strokes by inhibiting platelet aggregation.

Studies have shown that clopidogrel 75 mg is more effective than aspirin 325 mg in preventing recurrent stroke, myocardial infarction, and vascular death in patients with atherosclerosis [8]. Tranexamic acid, an antifibrinolytic, was administered within 72 hours to reduce the risk of rebleeding in patients at risk of aneurysm rupture, although its use carries a higher risk of cerebral ischemic events. Future studies should explore the combination of antifibrinolytics with other medications to mitigate vasospasm risks [8].

Amlodipine, a calcium channel blocker, was the most commonly used antihypertensive medication (40.48%). Blood pressure management is critical in stroke patients, particularly in those with comorbidities. In acute ischemic stroke, blood pressure is reduced cautiously, while in intracerebral hemorrhage stroke, intravenous antihypertensives are used with continuous monitoring [8]. Norepinephrine, a vasoconstrictor, was also used to maintain cerebral perfusion pressure in hemorrhagic stroke patients, with doses titrated based on blood pressure and perfusion targets [8].

Novorapid, a rapid-acting insulin analog, was used to manage blood glucose levels in diabetic stroke patients, with a target range of 100-150 mg/dL, as maintaining normoglycemia is essential in stroke therapy [2]. Diazepam was the most commonly used anticonvulsant (54.55%) for managing seizures in stroke patients, in line with national guidelines recommending intravenous diazepam followed by phenytoin for seizure control [8]. Omeprazole, a proton pump inhibitor (PPI), was frequently administered (28.15%) to prevent stress ulcers in elderly and severely ill stroke patients, with intravenous administration often used for more severe cases [8].

Finally, ringer's lactate was the most commonly used fluid therapy (85.93%). Intravenous fluids are essential for maintaining hemodynamic stability, but glucose or hypotonic fluids should be avoided to prevent complications. Instead, isotonic fluids such as saline are preferred for maintaining euvolemia [8].

Conclusion

The drug use patterns in stroke patients at Brebes Hospital revealed instances of irrational drug use, including drug selections that did not align with guidelines, contraindicated drugs, and medications prescribed without indication. There were one, five, and one occurrences of these issues, respectively. Addressing drug-related problems (DRPs) is crucial for optimizing stroke therapy, and pharmacists play a key role in resolving these issues to improve patient outcomes.

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Conflict of interest

The authors declare that they have no conflicts of interest related to the institutions involved in this research.

Author contributions

NAB: conceptualization, methodology, formal analysis, writing – original draft, writing – review & editing, supervision, project administration, corresponding author. IH: data curation, investigation, methodology, writing – review & editing. FSN: validation, visualization, resources, writing – review & editing.

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