Indonesian Journal of Global Health Research
Volume 7 Number 1, February 2025
e-ISSN 2715-1972; p-ISSN 2714-9749
http://jurnal.globalhealthsciencegroup.com/index.php/IJGHR

ANALYSIS OF THE RELATIONSHIP OF DRUG RELATED PROBLEMS (Drps) OF AMLODIPIN MEDICINE DOSAGE CATEGORY ON GERIATRIES' BLOOD PRESSURE ACCOMPLISHMENTS

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ABSTRACT
The increase in the number of geriatrics leads to an increase in health problems, one of which is related to hypertension. Hypertension is an important risk factor for cardiovascular disease morbidity and mortality that is often found in geriatrics. The class of drugs that are widely used to reduce blood pressure and have the potential to cause DRPs is the Calcium channel blocker (CCB) class of drugs, namely amlodipine. Objective: The purpose of this study was to analyze the relationship of Drug related problems (DRPs) in the single dose category in the use of amlodipine drugs to the achievement of geriatric blood pressure targets. Method: This study is a descriptive study using a cross-sectional observational design that is analytic in nature. Sampling using purposive sampling technique. The data analysis used was univariate and bivariate analysis. Result: The results showed that 70% of patients were female, 40% were over 70 years old and 70% of patients had stage 2 hypertension. There was 1 patient who experienced drug related problems (DRPs) in the drug dosage category with the result that the blood pressure target was not achieved and 1 patient who received the right dose of amlodipine with the result that the blood pressure target was not achieved. Conclusion: From the results of the study it can be concluded that there is no significant relationship between Drug Related Problems (DRPs) in the category of amlodipine drug dosage with the achievement of geriatric blood pressure targets ($p = 0.35$).

Keywords: amlodipine blood pressure; drug dosage; drug related problems (DRPS); geriatric

How to cite (in APA style)
Adiningsih, R., Anggraini, T. D., Andini, E. S., & Hapsari, E. D. (2024). Analysis of the Relationship of Drug Related Problems (DRPS) of Amlodipin Medicine Dosage Category on Geriatries' Blood Pressure Accomplishments. Indonesian Journal of Global Health Research, 7(1), 627-636. https://doi.org/10.37287/ijghr.v7i1.4858.

INTRODUCTION
In developed and developing countries, the increase in the elderly population is increasing. The increase in the elderly population is caused by a decrease in fertility (birth), mortality (death), and an increase in life expectancy (Maylasari S.ST, M.Si et al., 2017). According to the Central Bureau of Statistics (2021), it is projected that by 2045 the geriatric population in Indonesia will reach one-fifth of the population (Na DEC, 2021). The existence of physiological changes, pharmacokinetics, pharmacodynamics, as well as complications and polypharmacy in geriatrics causes problems related to drug use (Drug Related Problems) (Rahmawati, 2019).Hypertension is the leading cause of premature death worldwide. According to the World Health organization (WHO), an estimated 1.13 billion people worldwide suffer from hypertension, most of whom live in low- and middle-income areas (Haldar, 2013). According to the results of the 2018 Riskesdas, the incidence of hypertension in Indonesia is a health problem with a high prevalence of 34.1%. Hypertension also ranks 2nd out of 10 most common diseases in outpatients at hospitals in Indonesia with a prevalence of 4.67%. According to the annex of The Joint The National Committee (JNC 7) on Prevention, Detection, Evaluation and Treatment of High Bloodpressure, more than two-thirds of individuals after the age of 65 years experience hypertension (Chobanian et al.,

2003), while according to the Framingham Heart Study data, 55-year-old men and women without hypertension have a risk of developing hypertension at the age of 80 years, 93 and 91% respectively. In other words, at 55 years of age, more than 90% of people without hypertension will develop high blood pressure with age (Volpe et al., 2019).

Based on the Indonesian Health Survey (IHS) in 2023 and based on the 2011-2021 Non-Communicable Disease (NCD) cohort study, hypertension is included in the fourth category of diseases that have the highest risk of causing death at 10.2%. The prevalence of hypertension in Indonesia based on the 2018 Basic Health Research is 34.1% and in 2023 is 30.8%. There has been a decrease of about 3.3%, but this figure is still relatively high.The estimated occurrence of hypertension cases in Indonesia is 63,309,620 people while the number of death cases in Indonesia due to hypertension is 427,218 death cases. Central Java in 2020 has 2,542,187 cases of hypertension (Kementerian Kesehatan RI, 2017). Karanganyar Regency Primary Health Care and Traditional Health Services issued a list of the top 10 health center diseases as of 2023, hypertension is in second place with a total of 39,998 cases (Kementerian Kesehatan RI, 2023).

Drug related problems (DRPs) are an unexpected event from the patient's experience or suspected due to drug therapy that has the potential to interfere with the success of the desired cure (Cipolle) DRPs consist of reaction effects, drug selection, dosage, drug use and drug interactions (PCNE, 2020). The incidence of DRPs cases in the use of hypertension drugs has a relationship with not achieving optimal patient blood pressure targets (Pandiangan et al., 2017). The group of antihypertensive drugs that have the potential for DRPs is the Calcium Channel Blocker (CCB) group. Side effects of using high doses of amlodipine include orthostatic hypotension with reflex tachycardia (Ramadhan et al., 2015). Research conducted by Dzuriyah and Adiningsih in 2023 at UNS Sukoharjo Hospital stated that the group and type of hypertension drugs most widely prescribed were from the Calcium chanel blockers (CCB) group as many as 172 prescriptions (29.3%) with the type of hypertension drug that was widely prescribed from this group was Amlodipine as many as 136 drugs (23%) (Adiningsih, 2023)

Geriatric patients (>60 years old) are very susceptible to hypertension because age causes an increase in blood pressure. Geriatric patients experience thickening of the arterial chambers as well as collagen buildup in the muscle structure. Causing narrowing of blood vessels and stiffness (Azizah et al., 2018). Problems in the form of physiological changes, pharmacokinetics, pharmacodynamics, in geriatrics cause the risk of Drug Related Problems in the category of drug doses related to the achievement of geriatric blood pressure. Puskesmas as one of the front lines of health services for the Indonesian people should implement rational drug use according to existing standards. Inaccurate use of drugs at the health center level can be detrimental to the wider community. This study aims to determine the relationship of Drug Related Problems (DRPs) in the amlodipine drug dosage category to the achievement of geriatric blood pressure so that it can be used as a basis for appropriate drug selection policies in geriatrics.

METHOD

This research was conducted at the Mojogedang I Health Center, Karanganyar and has obtained an ethical feasibility letter from the Health Research Ethics Committee of Muhammadiyah Purwokerto University no KEPK/UMP/29/XI/2024.This study is a descriptive observational cross-sectional study that is analytic in nature with retrospective data collection. The population in this study were all elderly hypertensive patients at the

Mojogedang I Health Center, Karanganyar. Sampling using purposive sampling technique that meets the inclusion and exclusion criteria. Inclusion criteria include hypertensive patients aged ≥ 60 years, receiving amlodipine antihypertensive drugs in a single dose, patients with a single diagnosis of hypertension and patients who visit at least 3 times in 1 year. The exclusion criteria included patients who died and were referred to the hospital and patients who changed to other hypertension drugs. The materials used in this study were patient medical records containing patient identity including name, age, gender, diagnosis, examination results and data on patient drug use (amlodipine). The tools in this study are SPSS version 20 and research-related reference sources, namely JNC VIII, BNF 83 year 2022 and Drug Information Handbook (DIH).The research data were analyzed descriptively, univariate analysis for patient characteristics and bivariate analysis in the form of chi square statistical analysis to determine the relationship between 2 variables, namely the independent variable in the form of DRPs in the amlodipine drug dosage category with the dependent variable in the form of achievement of blood pressure targets with a 95% confidence level to determine the relationship between the two variables. The relationship is said to be meaningful if the significance value is less than 0.05

RESULT

Table 1.
Frequency Distribution of Patient characteristics

	f	%
Gender		
Male	3	30
Female	7	70
Total	10	100
Age		
60 – 64 years	3	30
65 - 69 years	3	30
>70 years	4	40
Total	10	100
Blood Pressure Classification		
Pre-Hypertension	1	10
Stage 1 Hypertension	2	20
Stage 2 Hypertension	7	70
Total	10	100

Table 2.
Patient Drug Dosage Conformity Data

No. Patient	Amlodipine dosage administered			Dosage based on BNF 83	Description
	Dosage	Frequency	Interval		
1	5 mg	1x day 1 tab	Every 24 hours	Amlodipine starting dose starts with 5mg once a day and a maximum of 10 mg per day.	Exactly
2	5 mg	1x day 1 tab			Exactly
3	5 mg	1x day 1 tab			Exactly
4	5 mg	1x day 1 tab			Exactly
5	5 mg	1x day 1 tab			Exactly
6	10mg	1x day 1 tab			Exactly
7	5 mg	1x day 1 tab			Exactly
8	5 mg	2x day 1 tab			Inappropriate
9	5 mg	1x day 1 tab			Exactly
10	5 mg	1x day 1 tab			Exactly

Table 3.
Patient Blood Pressure Target Achievement Data

No Patient	Initial Blood Pressure (mm/Hg)	Final Blood Pressure (mm/Hg)	Description
1	160/70	120/80	Achieved
2	150/80	120/80	Achieved
3	180/90	180/90	Not Achieved
4	140/80	120/80	Achieved
5	160/90	140/80	Achieved
6	220/100	150/90	Achieved
7	180/100	120/80	Achieved
8	120/80	120/80	Not Achieved
9	160/80	150/80	Achieved
10	170/90	140/90	Achieved

Table 4.
Results of Analysis of the Relationship between Age and Blood Pressure Classification

Age	Blood Pressure Classification			Total	p-Value
	Pre-Hypertension	Stage 1 Hypertension	Stage 2 Hypertension		
60-64	0	0	3	3	0,552
	0%	0%	100%	100%	
65-69	0	1	2	3	
	0%	33,3%	66,7%	100%	
>70	1	1	2	4	
	25%	25%	50%	100%	

Table 5.
Results of Analysis of the Relationship between Gender and Blood Pressure Classification

Gender	Blood Pressure Classification			Total	p-Value
	Pre-Hypertension	Stage 1 Hypertension	Stage 2 Hypertension		
Male	0	1	2	3	0,665
	0%	33,3%	66,7%	100%	
Female	1	1	5	7	
	14,3	14,3	71,4	100%	

Table 6.
Results of Analysis of the Relationship between Time to Take Medication and Achievement of Blood Pressure Targets

Dosage accurancy	Blood pressure achievement (mm/Hg)		Total	P-Value
	Not achieved	Achieved		
Morning	2	1	3	0,016
	66,7%	33,3%	100%	
Night	0	7	7	
	0%	100%	100%	

Results of Analysis of the Relationship between Drug Related Problems (DRPs) Drug Dosage Categories with Achievement of Patient Blood Pressure TargetsThe results of the analysis of the relationship between Drug Related Problems (DRPs) Drug Dosage Categories with Achievement of Patient Blood Pressure Targets are listed in table 7

Table 7.

Results of Analysis of the Relationship of Drug Related Problems (DRPs) Drug Dosage Category with Achievement of Blood Pressure Targets

Dosage accurancy	Blood pressure achievement		Total	P-Value
	Not achieved	Achieved		
Not the right dosage	1 100%	0 0%	1 100%	0,35
Correct dosage	1 11.1%	8 88.9%	9 100%	

DISCUSSION

Prescribing data for hypertension patients who met the inclusion and exclusion criteria in August-October 2024 were 10 patients. Patient data characteristics can be seen in table 1. The results showed that 70% of patients were female and 30% of patients were male. Women suffer more from hypertension when entering menopause due to a decrease in the hormone estrogen. When the amount decreases, endothelial cells will be destroyed because the estrogen content is depleted, endothelial damage triggers plaque in the blood while stimulating an increase in blood pressure (Wulandari, 2021) Women have a higher risk of suffering from hypertension than men. Especially when entering menopause due to hormonal factors (Khusna, 2021). In women who have menopause, it can be influenced by decreased levels of the hormone esterogen. The decrease in the hormone esterogen affects the increase in blood pressure through activation of the renin-angiotensin system (RAS) and the central nervous system. Angiotensin-II (A-II) is the main substrate of the RAS, a potent vasoconstrictor that causes constriction of blood vessels (Abramson, 2014).

The age of patients was classified into 3 groups, namely patients aged 60-64 years, 65-69 years and ≥ 70 years. The results showed that the most age suffering from hypertension was age ≥ 70 years as much as 40%. This is in line with research by Nuraeni (2019) which states that patients aged > 45 years have a higher risk than patients aged less than 45 years. Age is a factor that affects the increase in blood pressure. With increasing age, the arteries in the body will be prone to change. The accommodated blood capacity is reduced due to changes in wide and rigid blood vessels (Nuraeni, 2019). As age increases, changes occur in the arteries in the body to become wider and stiffer which results in reduced capacity and recoil of blood accommodated through the blood vessels. Aging also causes disruption of neurohormonal mechanisms such as the reninangiotensin-aldosterone system and also causes increased peripheral plasma concentrations and also the presence of glomerulosclerosis due to aging and intestinal fibrosis resulting in increased vasoconstriction and vascular resistance, resulting in increased blood pressure (hypertension) (Nuraeni, 2019).Based on the classification of hypertension, it was found that the most patients suffered from stage 2 hypertension as much as 70%, stage 1 hypertension as much as 20% and pre-hypertension as much as 10%. The results showed that stage 2 hypertension was mostly suffered by patients aged> 70 years. Stage 2 hypertension can cause long-term damage to the heart and blood vessels. Conditions of increased systolic blood pressure need to be a concern, especially in the elderly (James et al., 2014).

Evaluation of Drug Related Problems (DRPs) Dose Selection Category

The results of the study are listed in table 2 and obtained the results of 1 discrepancy in the administration of amlodipine drugs, namely in patient number 8 who received amlodipine 5mg therapy with a frequency of use 2 times a day 1 tablet. This is not in accordance with the standards set by BNF 83, namely the initial dose of Amlodipine starting with 5mg once a day

and a maximum of 10 mg per day. Amlodipine was taken after meals at night. The use of amlodipine at night provides an effective effect in reducing blood pressure. Amlodipine is given once a day because it has a long duration of action (Khusna, 2021). Drug administration is said to be the right dose if it meets 3 accuracies, namely the right dose, the right frequency and the right interval of drug use. Amlodipine is one of the first-line antihypertensive drugs in elderly patients based on JNC VIII and recommended by the Indonesian Cardiovascular Medical Association (PERKI) in 2015 and the Indonesian Society of Hypertension Physicians (PERHI) in 2019 (Sayyidah, Hasan & Ulumudin, 2020). Amlodipine works by inhibiting calcium ions through slow-acting channels in the cell membrane. This drug is very suitable for use in the elderly because it can reduce systolic hypertension so as to reduce the risk of severe organ damage due to the disease and also the risk of cardiovascular events (Khusna, 2021). Amlodipine is considered to have good clinical management of hypertension, as it has been shown to be effective and safe in lowering blood pressure with good tolerance. Amlodipine is also more recommended in patients with essential hypertension, renovascular hypertension, hypertension in the black race, hypertension with diabetes mellitus, hypertension with bronchial asthma and hypertension with left ventricular hypertrophy. The antihypertensive effect of amlodipine is dose-related, if the dose is increased, the antihypertensive effect is greater (Aziza, 2007). In addition, amlodipine also has a long duration of action so that it is enough to be given once a day and is very useful for treating emergency hypertension in a short time (Susilowati & Risnawati, 2017).

Data Analysis of Blood Pressure Target Achievement

Table 3 shows the patient's baseline blood pressure and final blood pressure at 3-month intervals. According to JNC VII, once antihypertensive drug therapy is started, most patients should return for follow-up and drug adjustment every month or until the blood pressure target is achieved. More frequent visits are required for patients with stage 2 hypertension or with complicated comorbid conditions. Serum potassium and creatinine should be monitored at least one to two times per year. Once the blood pressure has reached target and stabilized, follow-up visits can usually be done at 3 to 6 month intervals. There were 2 patients who did not achieve their blood pressure targets, namely patient no 2 in the stage 2 hypertension category and patient no 8 in the pre-hypertension category. Treatment of stage II hypertension can be either single or combination depending on the patient's condition. Risk factors that can affect therapy are patient age, comorbidities, the dose of drugs given, and drug interactions (James et al., 2014).

Analysis of the Relationship between Age and Blood Pressure

The table obtained the p value is 0.552 greater than ($p < 0.05$) which means H0 is accepted. It can be concluded that there is no significant relationship between age and blood pressure. The absence of a relationship between age and blood pressure can be caused by other factors, namely directly influenced by food intake and an unhealthy lifestyle. Elderly patients are not compliant with routine follow-up, resulting in a vacuum of antihypertensive drugs which causes the target blood pressure not to be achieved and the possibility becomes greater. Non-compliance with control in patients can be caused by several factors including limited medical costs, long distances from the patient's home to health services (Syarifah N Y R S Assegaf & Ulfah, 2022).

Analysis of the Relationship between Gender and Blood Pressure

The table results obtained a p value of 0.665 greater than ($p <0.05$) which means H0 is accepted. Therefore, it can be concluded that there is no significant relationship between gender and blood pressure in patients at the Mojogedang I Health Center, Karanganyar. The

absence of a relationship is influenced by stress. Elderly people who experience psychosocial stress have a risk of developing hypertension 2.54 times greater than the absence of psychosocial stress (Handayani D S, Rusli et al., 2016).

Analysis of the Relationship between Medication Taking Time and Blood Pressure Target Achievement

The results of Table 6 obtained a p value of 0.016 smaller than ($p < 0.05$) which means H0 is rejected. Therefore, it can be concluded that there is a significant relationship between the time of taking medication and the patient's blood pressure. The results showed that there were 7 patients prescribed amlodipine with a nighttime drinking time that achieved the blood pressure target. This is related to pharmacology in which the circadian rhythm of blood pressure reaches a peak at 6 to 12 am, the level of amlodipine in the blood is close to the maximum level (ie 5- 5.8ng/mL, after being taken 6-12 hours) when taken at night (at 18.00) amlodipine can reduce blood pressure just when the blood pressure reaches its peak. So that the administration of amlodipine at night (after 18.00) reduces systole and diastole blood pressure significantly more than amlodipine given in the morning (before 12.00) (Zhang et al., 2021).

Analysis of the Relationship of Drug Related Problems (DRPs) Category of Drug Dose Selection with Achievement of Geriatric Blood Pressure Targets

The results of the table show that the p value of 0.35 is greater than ($p < 0.05$), which means that H0 is accepted. It can be concluded that there is no significant relationship between Drug Related Problems (DRPs) in the category of drug dose selection and the achievement of blood pressure targets. geriatrics. There was 1 patient in the stage 2 hypertension category who received the right dose of amlodipine but did not reach his blood pressure target. factors that affect the achievement of blood pressure targets in patients are related to patient non-compliance in taking hypertension drugs. Patients in the pre-hypertension category had 1 patient who experienced drug related problems in the drug dosage category where the patient took amlodipine 2 times a day, which means taking the drug with excessive frequency, and the results did not reach the blood pressure target. The occurrence of DRPs of excessive frequency occurred in patients who received Amlodipine 2 times a day 1 tablet (Table 2). Based on the recommended dose in DIH (2018) and BNF 83, the frequency of using Amlodipine as an antihypertensive is once daily dose, which is 5 mg/day as the initial dose and can be increased to 10 mg/day if needed. Giving amlodipine 2 times a day 5 mg does not actually exceed the maximum dose set, but it is considered ineffective and does not provide additional benefits.

These results are in line with the research of (Miyoshi et al., 2013) which states that the administration of amlodipine in two divided doses is not associated with increased plasma concentrations of amlodipine, does not reduce arterial stiffness, and does not improve blood pressure control within 24 hours in patients with essential hypertension. The occurrence of DRP can cause ineffective therapy so that it can affect the patient's therapeutic outcome, namely by not achieving blood pressure targets. Not achieving the therapy target can be caused by other factors or other categories of DRPs. Apart from the presence of DRPs in therapy, there are other factors that can affect the rise and fall of blood pressure. The presence of other comorbidities suffered, the patient's age, gender, body position, excess weight (obesity), stress conditions or psychological conditions, and previous unhealthy lifestyles can affect blood pressure reduction in accordance with therapeutic targets (Marhaendra et al., 2016). The blood pressure lowering effect of amlodipine begins within 2 to 4 hours after consumption. Amlodipine takes 6 to 12 hours to reach its peak blood pressure lowering effect.

A more consistent reduction in blood pressure over 24 hours is the therapeutic effect of the 10 mg dose of amlodipine. Therefore, amlodipine is an effective drug to control blood pressure better in the long term (Li X et al., 2018).

CONCLUSION

From the results of the study, it can be concluded that there is no significant relationship between Drug Related Problems (DRPs) in the amlodipine drug dosage category and the achievement of geriatric blood pressure targets (p = 0.35).

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