

Prescribing patterns of anti-hypertensive medications at PHC clinic Pedurungan, Semarang

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Abstract

Hypertension is one of the leading causes of premature death worldwide and can cause complications such as stroke, coronary heart disease and kidney failure. The number of hypertension sufferers in 2018 was higher than in 2013 at 8.31%. Control of hypertension includes non-pharmacological therapy and pharmacological therapy. Pharmacological treatment must be supported by adequate drug availability, so knowing the drug prescribing pattern in a health facility is necessary. This study aims to determine the design of antihypertensive prescribing at the Pedurungan PHC Clinic, Semarang. This research is a type of descriptive observational study using retrospective data in the form of prescription sheets containing antihypertensives from October to December 2022. The data taken in this study were age, gender, antihypertensive name, and number of antihypertensive items. Data were analyzed by classification according to gender, age, antihypertensive name, antihypertensive combination, and antihypertensive group, and quantitatively by calculating the percentage. The results showed 137 prescriptions with 187 antihypertensive agents within the period. Hypertension in women was higher than in men (52.83%). The highest prevalence of hypertension was 56 – 65 years old. The pattern of prescribing resulted in the monotherapy being higher than combination therapy. Amlodipine 10 mg (28.26%) was the most widely used in a single treatment. The antihypertensive groups showed that calcium channel blockers had the highest presentation (49.63%) while angiotensin-converting enzyme inhibitors were used the least, namely 2.19%. The most widely used antihypertensive combination therapy is a combination of two types of antihypertensive groups, namely calcium channel blockers and angiotensin receptor blockers, with a percentage of 15.33%. This research concluded that monotherapy was more used than combination therapy, and amlodipine 10 mg was the highest presentation in hypertension patients at PHC Clinic, Pedurungan, Semarang.

Keywords: *prescribing patterns; antihypertensive ; agents ; PHC Clinic*

Introduction

Hypertension is a non-communicable disease that is one of the leading causes of premature death worldwide. Data from the World Health Organization in 2018 shows that the global prevalence of hypertension is 22% of the world population. Southeast Asia is in the third-highest position, with a prevalence of 25% of the total population (Ministry of Health, Republic of Indonesia, 2019). The survey shows that in Indonesia, the prevalence of hypertension starting from the age of 18 was 34.11% in 2018. This prevalence was higher than in the survey in 2013, namely 25.8%, so the total increase in hypertension prevalence was 8.31% (Ministry of Health Republic of Indonesia, 2018). Age ≥ 35 , the risk of developing hypertension increases with age. Systolic pressure increases by an average of 20 mmHg and continues to increase after the age of 70 years because, with increasing age, the body's abilities and mechanisms decrease slowly, one of which is an increase in peripheral vascular resistance (obstruction of blood flow in peripheral blood vessels) in arteries (Calvin, 2018).

Hypertension can be divided into two types: hypertension of unknown cause (primary hypertension) and hypertension of known cause (secondary hypertension). The symptoms of hypertension are almost like other diseases, such as dizziness, headaches, and blurred vision, so most hypertension sufferers are unaware of their disease. Risk factors for hypertension that cannot be changed include heredity (genetics), age and gender. In contrast, risk factors that can be changed include lifestyle-related factors such as smoking, alcohol consumption, lack of physical activity, consumption of foods high in sodium, low consumption of fruit and vegetables, stress and obesity (Ministry of Health Republic of Indonesia, 2018).

Hypertension threatens public health because it can potentially cause complications such as stroke, coronary heart disease and kidney failure (Dipiro *et al.*, 2015). Hypertension must be controlled to prevent and reduce morbidity, complications, and death. These steps can be grouped into pharmacological and non-pharmacological approaches. Non-pharmacological approaches to lower blood pressure are losing weight, reducing stress, not smoking, avoiding alcohol, and doing sports activities, which can also reduce blood pressure (Fauziah, 2021), and limiting salt intake to less than 5 grams per day (WHO, 2012).

Pharmacological approaches are carried out with antihypertensive medication therapy. Antihypertensives are divided into several groups, namely diuretics, beta blockers, alpha II adrenergic agonists, calcium antagonists (Calcium channel blockers/CCB), Angiotensin-converting enzyme inhibitors (ACE-Inhibitors), Angiotensin receptor blockers (ARB) (BPOM RI, 2014). Initial treatment for hypertensive patients can begin by controlling blood pressure regularly

and periodically checking their health at the health center, clinic or hospital at least once a month (Ministry of Health Republic of Indonesia, 2019).

PHC Clinic, Pedurungan, Semarang, is a clinic that provides health services supported by diagnostic medical procedures and drug services. Every month, an average of 662 prescriptions are received at the pharmacy, and 117 (18%) prescriptions contain antihypertensives. Hypertension treatment is long-term treatment, even for life. Patients are required to take medication regularly even if there are no symptoms. The availability of antihypertensives in pharmacies or clinics must be guaranteed. Based on this background, research must be conducted on antihypertensive prescribing patterns at the PHC Clinic, Pedurungan.

Methods

This type of research is descriptive observational research using retrospective data. The data used in the research were obtained from patient prescription sheets containing antihypertensives in October – December 2022 at the PHC Clinic, Pedurungan, Semarang. The data taken in this study were the date and number of prescriptions, patient characteristics (age and gender), type of antihypertensive and number of antihypertensive items. The data obtained were analyzed qualitatively to be classified according to gender, age, antihypertensive, combination of antihypertensives and antihypertensive group. Data was also processed quantitatively by calculating the percentage.

Results and Discussions

The Characteristics of the Patient

Based on data obtained from antihypertensive prescriptions at the PHC Clinic in October – December 2022, there were 137 prescriptions. The data is then processed quantitatively and qualitatively. The collected data was analyzed qualitatively to be classified according to gender, age, type of antihypertensive, combination of antihypertensives and antihypertensive group. The distribution of patients based on gender and age can be seen in **Table 1**.

Table 1. The characteristics of hypertension patients in October – December 2023 at PHC Clinic.

No.	Range of Age (years)	The number of patients		Percentage (%)		Total (%)
		Men	Women	Men	Women	
1.	35 - 45	14	4	10,22	2,92	18 (13,14)
2.	46 - 55	12	8	8,76	5,84	20 (14,60)
3.	56 - 65	9	28	6,57	20,44	37 (27,01)
4.	> 65	32	30	23,36	21,89	62 (45,25)
Total		67	70	48,17	51,83	137 (100)

In Table 1, it is found that the distribution of hypertensive patients at the PHC Pedurungan Semarang Clinic shows a relatively significant increase in the number of female patients in the range 56 – 65 years old, namely 20.44%, wherein the 35 – 45 year age range there are only 2.92% of patients. This result was influenced by menopause, which generally occurs at 45-55 years (Purnama, 2017). Levels of the hormone estrogen influence the incidence of hypertension one estrogen. In women, the hormone estrogen plays a role in increasing High-Density Lipoprotein (HDL) levels. HDL cholesterol is a protective factor in preventing the atherosclerosis process. The protective effect of estrogen in women prevents the risk of hypertension. The estrogen hormone levels will decrease when women enter menopause, so women become more susceptible to hypertension (Kusuma *et al.*, 2016). The number of male patients begins to increase in the age range of 35-45 years, in line with research by Aristotle (2018) in Palembang, which shows that gender influences the incidence of hypertension. Hypertension in men can be triggered by unhealthy lifestyle behaviors such as smoking and psychological factors that cause stress.

The total number of hypertensive patients aged > 65 years has increased. This shows that hypertension is a degenerative disease that tends to get worse over time due to decreased function of the body's organs. According to the data in the research above, the older the number of hypertensive patients increases. This shows that the risk of hypertension increases because as you get older, your blood vessels experience changes in structure, becoming stiffer, which tends to cause higher pressure. After all, blood is forced through the vessel's narrow blood (Adam, 2019).

The Prescribing Patterns of Antihypertensive

Data obtained from 137 prescriptions contained 184 antihypertensive items. The percentage of antihypertensives based on drug type at the PHC Pedurungan Semarang Clinic for October - December 2022 can be seen in **Table 2**.

Table 2. The Prescribing Patterns based on the antihypertensive drugs.

No.	The name of drugs	Drugs potency (mg)	The number	Percentage (%)
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1.	Amlodipine	10	52	28,26
2.	Amlodipine	5	43	23,37
3.	Candesartan	16	15	8,15
4.	Candesartan	8	11	5,98
5.	Valsartan	80	11	5,98
6.	Spirolactone	25	9	4,89
7.	Bisoprolol	2,5	8	4,35
8.	Bisoprolol	5	8	4,35
9.	Furosemide	40	8	4,35
10.	Irbesartan	300	5	2,72
11.	Nifedipine	30	5	2,72
12.	Losartan	50	2	1,09
13.	Captopril	25	1	0,54
14.	Carvedilol	6,25	1	0,54
15.	Clonidine	0,15	1	0,54
16.	Imidaprilat	5	1	0,54
17.	Olmesartan	40	1	0,54
18.	Ramipril	10	1	0,54
19.	Telmisartan	80	1	0,54
Total			184	100

Table 2 shows that amlodipine 10 mg and amlodipine 5 mg have a usage percentage of more than 20% of the total antihypertensive items. Amlodipine 10 mg is the most widely used because blood pressure targets are not achieved in the first treatment, so that the initial drug dose can be increased. Amlodipine is the most frequently prescribed CCB group because it is relatively affordable. It also has the advantage of its pharmacodynamic and pharmacokinetic properties.

Amlodipine has a long half-life with a duration of lowering blood pressure for 24 hours, high bioavailability and a long duration of drug action, allowing for once-a-day dosing (Chan *et al.*, 2016). Administration of amlodipine is recommended at night because it can reduce the risk of death, the risk of type 2 diabetes and the routine of waking up due to the habit of most people who tend to take medication before bed. This can benefit patient compliance in taking medication (Admaja, 2020). Amlodipine has a working mechanism of relaxing blood vessel arterioles. Amlodipine is vascular-selective, preventing blood pressure from dropping suddenly (Tandililing *et al.*, 2014). Based on the data collected, the percentage of antihypertensives based on the group at the PHC Pedurungan Semarang Clinic for October – December 2022 can be seen in **Table 3**.

Table 3. The number of antihypertensive drugs in October – December 2022 at PHC Clinic.

No.	The antihypertensive groups	The number	Percentage (%)
1	Calcium channel blocker (CCB)	100	54,35
2	Angiotensin receptor blocker (ARB)	46	25,00
3	Beta Blocker	17	9,24
4	Diuretic	17	9,24
5	ACE Inhibitor	3	1,63
6	Agonis α II adrenergic	1	0,54
Total		184	100

The percentage of the antihypertensive class that is most widely used is the CCB group at 54.35%. This is in line with research by Andriyana (2018), which states that the antihypertensive often prescribed for elderly patients is Amlodipine, which is included in the CCB group as much as 32.78%. The CCB group is often used as therapy for elderly patients because it is a class of antihypertensives that has good clinical management of hypertension either alone or in combination and has been proven to be safe and effective in lowering blood pressure with good tolerance (Ardhany *et al.*, 2018). This is also in line with research by Alaydrus and Tobing (2019), which explains that as many as 60% of the antihypertensive therapy chosen is Amlodipine, which is included in the CCB group for elderly patients because the use of CCB class antihypertensives has a working mechanism by relaxing the heart muscle and smooth muscle by inhibiting calcium activity or inhibiting the flow of calcium into the heart muscle and arterial blood vessel

walls (Dipiro *et al.*, 2015). The CCB group provides more vasodilation benefits in arterial blood vessels, so it is effective for use in elderly patients because, in the elderly, there is stiffness of the blood vessels (Mason, 2012).

The use of α II adrenergic agonist antihypertensives is the lowest in percentage because the mechanism of action of this group is directly on the central nervous system, inhibits the action of hormones, can reduce sympathetic nerve activity, affects smooth muscle function, which can cause side effects, unusual fatigue or depression, sexual dysfunction, and sleep disorders, including nightmares (Ministry of Health Republic of Indonesia, 2019). The collected data was grouped, and the percentage of antihypertensive types obtained based on single and combination administration can be seen in Table 4. Table 4 shows more antihypertensive administration when a single therapy is administered (71,53%). Pharmacological therapy for hypertension begins with a single drug because monotherapy can reduce systolic blood pressure by around 7-13 mmHg and diastolic blood pressure by around 4-8 mmHg. After receiving therapy within one month, if the blood pressure target is not achieved, the initial drug dose can increase. Adding other drug classes from first and second-line therapy can minimize the side effects of drug interactions (Putri *et al.*, 2019). Monotherapy administration is given to patients whose blood pressure tends to be better controlled. Patients with high levels of compliance with antihypertensive use show better blood pressure control than those with low compliance. Giving antihypertensives in a single form is generally because the patient is still in the early stages of treatment for stage 1 hypertension. This is in line with research presented by Sinata and Rahmadani (2021) regarding the description of the use of antihypertensives at the Sidomulyo Outpatient Health Center Pekanbaru in 2020.

Table 4. The Patterns of Antihypertensive Prescription in October – December 2022 at PHC Clinic, Pedurungan, Semarang.

Type of therapy	Type of groups	The number	Percentage (%)	Total (%)	
Monotherapy	CCB	68	49,63	71,53	
	ARB	13	9,49		
	Diuretic	7	5,11		
	Beta Blocker	7	5,11		
	ACE Inhibitor	3	2,19		
Combination	CCB + ARB	21	15,33	24,09	
	CCB + Betablocker	3	2,19		
	CCB + Diuretic	3	2,19		
	ARB + Betablocker	3	2,19		
	ARB + Diuretic	3	2,19		
	2	CCB + ARB + Betablocker	2	1,46	3,65
		CCB + ARB + Diuretic	2	1,46	
		ARB + Betablocker + Diuretic	1	0,73	
	3	CCB + ARB + Betablocker + Diuretic	1	0,73	0,73
		ARB + Betablocker + Diuretic	1	0,73	
5	CCB + ARB + Betablocker + Agonis α II + Diuretic	1	0,73	0,73	
Total		137	100	100	

The use of single antihypertensives at the PHC Pedurungan Semarang Clinic is mainly in the CCB group (49.63%). In line with this research, hypertension is mainly experienced by elderly patients because CCB has a working mechanism that provides more vasodilation benefits in arterial blood vessels, so it is effectively used in elderly patients because, in the elderly, there is stiffness of the blood vessels (Mason, 2012). CCB can also inhibit voltage-sensitive calcium channels, thereby reducing the entry of extracellular calcium into heart cells and blood vessel walls (Dipiro *et al.*, 2015). The ACE Inhibitor group is the least prescribed, namely (2.19%), because the side effects of these drugs can cause dry cough, weakness, dizziness or headaches, and increased blood potassium levels, so ACE Inhibitors are rarely chosen as therapy, especially in elderly patients (Ministry of Health Republic of Indonesia, 2019).

Table 4 also shows that the two-combination therapy is the most widely used in the patient. It is ARB and CCB. The Joint National Committee (JNC) VIII suggests that selecting the type of drug combination needs to consider the patient's clinical condition. A combination of two antihypertensives is given to stage 2 or stage 1 hypertension patients who do not reach the blood pressure target with a single administration of antihypertensives. It aims to lower blood pressure and help reduce the side effects of drug use when compared to using high-dose single antihypertensive therapy. Combination therapy is an option for patients who find it challenging to achieve blood pressure targets or for patients with many indications who require several antihypertensives (Ansa *et al.*, 2010). Combination therapy can use two or more different classes of antihypertensives depending on the patient's clinical condition. The combination of CCB and ARB (15,33%) is more often given to hypertensive patients because it is well tolerated at the beginning of treatment and is superior in inhibiting renin-angiotensin aldosterone stimulation (RAAS), as well as reducing oxidative stress and arterial rigidity, reducing the risk of stroke progression and vascular dementia (Putri *et al.*, 2019). The combination of CCB and ARB has the advantage of lowering blood pressure and preventing high-risk cardiovascular events in

hypertensive patients (JNC-8, 2013). The same thing was also stated that CCB does not increase the incidence of mortality in CKD patients, so the combination of ARB and CCB can be a therapeutic option to be considered to obtain a better antihypertensive effect and cause lower metabolic events (Kinanti *et al.*, 2022).

CCB has a working mechanism that inhibits the movement of calcium from blood vessels to the heart muscle and smooth muscle and can reduce peripheral resistance so that blood pressure can decrease. In contrast, ARB has a working mechanism by directly inhibiting angiotensin II type I receptors to reduce blood pressure. These ARBs have milder side effects, such as ACE inhibitors, than other groups. The combination of CCB + ARB is effective because the incidence of peripheral edema due to CCB use can be overcome by ARB with joint vasodilation of veins and arteries so that blood pressure can be reduced and side effects can be suppressed (Wulandari *et al.*, 2021).

Based on a combination of three types of antihypertensives at the Pedurungan PHC Clinic, Semarang, for October – December 2022, which can also be seen in Table 4. The distribution of types of antihypertensives based on the combination of three drug items shows that data on most combinations use the CCB, ARB, Betablocker and CCB, ARB, Diuretic groups (1,46%). The combination of three types of drugs can indicate that the patient is suffering from stage 2 hypertension and does not reach the blood pressure target with the combination of two antihypertensives, especially in patients with compelling indications that aim to avoid further organ damage (Pikir *et al.*, 2015). Choosing the type of combination must also pay attention to the patient's comorbidities so that the right group can be selected, such as an effective ARB for hypertensive patients with kidney disorders, an effective ACE inhibitor for hypertensive patients with accompanying diabetes mellitus, an effective Betablocker for hypertensive patients with impaired heart function (Ansa *et al.*, 2010). The background patients with a combination of three antihypertensives have comorbidities with impaired heart function, so it is necessary to add beta-blocker and diuretic antihypertensives. The purpose of adding Betablocker to the combination of CCB and ARB aims to slow the heart rate and reduce the pressure on the heart muscle when it beats while having the effect of widening the blood vessels, resulting in a decrease in blood pressure and a reduced burden on the heart in pumping blood throughout the body (Sari *et al.*, 2020).

The addition of diuretics to the combination of CCB and ARB is to control blood pressure by inhibiting the absorption of sodium, chloride and potassium salts and releasing more salt and water from the blood vessels into the urine. Blood pressure can be reduced by reducing the amount of fluid in the blood vessels (Fa'idah, 2016). Diuretics can also inhibit vasoconstriction (narrowing) of blood vessels so that blood vessels become loose and can reduce blood pressure (Ministry of Health, Republic of Indonesia, 2019).

Table 4 also shows that only one patient took five antihypertensive drugs (0,73%). This could indicate the presence of persistent hypertension. Persistent hypertension is blood pressure that does not reach the target BP <140 mmHg and BP <90 mmHg, even though you have received three or more types of antihypertensives of different classes at the maximum dose, and the patient has carried out lifestyle modification recommendations (Ministry of Health Republic of Indonesia, 2019). The background patients who received a combination of five antihypertensives in this study had other comorbidities, such as hypercholesterolemia and diabetes mellitus. Cases of diabetes mellitus with uncontrolled blood sugar can cause damage to small and large blood vessels, which triggers plaque formation in the blood vessels or atherosclerosis. This triggers blood to thicken, making the heart work harder and increasing blood pressure so that up to five antihypertensives are needed in combination (Mandaya, 2021).

The addition of α II agonists to the combination therapy of CCB, ARB, Betablocker and Diuretic is an antihypertensive that stimulates alpha-2 adrenoceptor receptors in the central nervous system (brain and spinal cord). Alpha-2 receptors are found on cells in the sympathetic nervous system. When alpha-2 receptors are stimulated, there is an obstacle to releasing norepinephrine, which reduces sympathetic activity. This plays a role in widening blood vessels to reduce blood pressure (Ministry of Health, Republic of Indonesia, 2019).

For hypertensive patients with comorbid diabetes mellitus, adding Betablocker is not recommended because it can have a camouflage effect on diabetes mellitus levels or mask the side effects of hypoglycemia from antidiabetic drugs but can be given as a last resort for patients who also experience impaired heart function or heart failure, in patients Betablocker heart can maintain the stability of the heart rhythm and muscle (Dungan *et al.*, 2019).

Conclusions

The pattern of antihypertensive prescribing at the PHC Pedurungan Semarang Clinic for the period October – December 2022 shows that most hypertension therapy uses a single therapy (71.53%), the most widely used group is the CCB group (49,63%), the most widely used antihypertensive was amlodipine 10 mg (28.26%). The suggestions given by this research can still be developed further by looking at the effectiveness of therapy (the success of therapy after one month or more of antihypertensive use).

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