

THE APPLICATION OF ANATOMICAL THERAPEUTIC CHEMICAL METHOD TO EVALUATE THE USE OF ANTI-HYPERTENSION DRUGS IN INPATITION INSTALLATIONS OF REGIONAL GENERAL HOSPITALS

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Abstrak

Tujuan dari penelitian ini adalah untuk mengetahui jenis dan proporsi obat antihipertensi yang diminum oleh pasien hipertensi yang dirawat di rumah sakit. Metodologi penelitian deskriptif cross-sectional digunakan dalam penelitian ini. Semua pasien hipertensi yang dirawat di rumah sakit menjadi populasi penelitian. Purposive sampling dengan menggunakan sistematik random sampling digunakan dalam penelitian ini untuk mendapatkan 100 sampel. Penelitian retrospektif, atau penelitian berdasarkan rekam medis pasien, digunakan untuk memperoleh data untuk penelitian ini. Analisis univariat dan pendekatan DDD/ATC akan digunakan untuk menilai analisis data yang dilakukan dengan menggunakan aplikasi Microsoft Excel. Ada beberapa kesimpulan yang dapat diambil dari temuan penelitian ini: Berdasarkan usia dan jenis kelamin, mayoritas pasien hipertensi adalah perempuan. Stroke iskemik merupakan penyakit penyerta yang paling banyak dialami oleh penderita hipertensi, sesuai dengan jenis penyakit penyertanya. Kebanyakan pasien hipertensi mempunyai tekanan darah sistolik kurang dari 160 mmHg dan seringkali mempunyai tekanan darah diastolik kurang dari 100 mmHg. Amlodipine terbukti menjadi obat antihipertensi yang paling sering digunakan oleh pasien hipertensi, diukur dari jumlah penggunaan. Amlodipine, ramipril, captopril, dan irbesartan adalah obat antihipertensi yang termasuk dalam sebagian besar bagian DU, menurut profil DU mayoritas. Obat antihipertensi yang digunakan sesuai dengan formularium rumah sakit.

Kata kunci: Obat Antihipertensi, Pasien Hipertensi, Rumah Sakit.

Abstract

The purpose of this study is to identify the kinds and proportions of antihypertensive medications taken by hypertension patients who are hospitalized. Cross-sectional descriptive research methodology is used in this study. All hospitalized hypertension patients made up the study's population. Purposive sampling using systematic random sampling was used in this study to get 100 samples. Retrospective research, or research based on patient medical records, was used to acquire the data for this study. Univariate analysis and the DDD/ATC approach will be used to assess data analysis performed using the Microsoft Excel application. There are a number of inferences that may be derived from the study's findings: According to age and gender, women make up the majority of hypertension patients. Ischemic stroke is the most common comorbidity that hypertension people experience, according to the kind of comorbidity. Most hypertension patients have systolic blood pressure of less than 160 mmHg and often have diastolic blood pressure of less than 100 mmHg. Amlodipine was shown to be the antihypertensive that was used by hypertension patients the most frequently, measured by the number of uses. Amlodipine, ramipril, captopril, and irbesartan are the antihypertensive medications included in the majority DU section, according to the majority DU profile. Antihypertensive medications are used in accordance with the hospital formulary.

Keywords: Antihypertensive Drugs, Hypertensive Patients, Hospital.

INTRODUCTION

An increase in systolic blood pressure of more than 140 mmHg and a diastolic blood pressure increase of more than 90 mmHg in two tests with a five-minute gap between them indicate the presence of hypertension. Because most people are unaware they have hypertension prior to having their blood pressure monitored and because problems from hypertension typically do not manifest as signs or symptoms, hypertension is frequently referred to as the silent killer (Carter et al., 2003). Around 900 million individuals worldwide, or 27% of the population, have hypertension. In 2025, this percentage is probably going to rise to 29%. Of the 900 million people who have hypertension, 34%

live in developed nations, and the remainder do, including Indonesia. In over 93% of cases, the etiology is unknown, though (Susanto, 2023). According to data from 2012 to 2015, 82% of people with hypertension were aware that they had the condition; 75% received treatment; 53% of patients had their blood pressure under control (systolic and diastolic readings of less than 140 and 90 mmHg, respectively); and 48% did not (Achmad et al., 2021). One of the leading causes of mortality and morbidity in Indonesia is hypertension. In Indonesia, 25% of people under the age of 18 who have hypertension are over the age of 26, which is a high number. Only 10%, though, had received a medical diagnosis or had previously taken medicine. This suggests that the majority of community members who have hypertension have not received a diagnosis or access to healthcare (Bahua, 2016).

In general, blood pressure rises as we become older. 90% of those under 55 who previously had normal blood pressure are at risk of developing hypertension (Suparwata, 2018). Most patients had prehypertensive blood pressure before they were diagnosed with hypertension, and most were diagnosed with hypertension between the ages of the third and fifth decades (Amelia et al., 2021). The 2020 Indonesian health data profile stated that hypertension was one of the 10 diseases with the most cases of hospitalization in 2020, with a proportion of cases of 42% of men and 58% of women, and 5% of patients died. Hemorrhagic stroke, coronary and ischemic heart disease, and hypertension are all key risk factors (Joseph et al., 2008). With a beginning blood pressure of 115/75 mmHg, every 20/10 mmHg increase in blood pressure doubles the risk of cardiovascular disease in particular age groups (Rafli et al., 2021). Heart failure, peripheral vascular disease, kidney issues, retinal hemorrhages, and vision issues are additional complications brought on by hypertension in addition to coronary heart disease and stroke. In order to lower the risk of cardiovascular disease, hypertension medication must be used to lower systolic and diastolic blood pressure to less than 140/90 mmHg (GS et al., 2022).

To obtain the best blood pressure control, a more thorough and extensive strategy is required. In order to carry out their professional practices at every site where a health service is provided, pharmacist colleagues must actively participate in order to reach this goal (Susanto, 2021). In addition to educating patients about hypertension, pharmacists can also monitor patient response through community pharmacies, assure compliance with drug and non-drug therapy, identify and minimize adverse effects, and prevent or address issues with drug administration. In addition, pharmacists, particularly those employed by hospitals, can offer clinical pharmacy services in compliance with the Pharmaceutical Service Standards in Hospitals (Altaf et al., 2014). The assessment of drug use is one of the clinical pharmacy services that can be offered. Drug usage needs to be assessed in order to determine whether the drugs will be safe and effective given the patient's condition (Anggraini & Hasni, 2021). There are two types of drug use evaluation: qualitative and quantitative. The Anatomical Therapeutic Chemical/Defined Daily Dose (ATC/DDD) technique will be used in one quantitative investigation. The WHO advises using this approach to assess drug use. The ATC/DDD system is a classification and measurement system for drug use that has currently become a center of attention in the development of drug use research (Anggraini et al., 2022).

The ATC classification and DDD method are commonly used to compare drug consumption between countries because they can reflect global drug doses without being influenced by the genetic variations of each ethnicity (Hasni et al., 2016). The calculation of DDD/100 patient days or DDD/100 bed days is the most advised when used in a hospital setting. DDD/100 inhibitions per day or DDD per inhibition per year are typically used for computations between nations. The aim of the ATC/DDD method is to use it as a means of research on drug use to improve the quality of drug use. One of these components is a comparison of drug consumption at the international level or between health service systems. A comparison of drug use is useful to determine any differences (Alfalah et al., 2022). Further evaluation is carried out when significant differences are found, leading to the identification of problems and improvements to the drug use system (Susanto, 2010). A further development of the DDD method is Drug Utilization 90% (DU 90%). DU 90% shows the number of drugs whose use reaches 90% of all drugs prescribed after calculating DDD; the remaining are certain drugs used for conditions that rarely occur in patients with a history of drug intolerance or side effects (Susanto, 2011). The DU method has been proposed as a single method for generally assessing the quality of prescribed drugs (Fadlilah et al., 2022). The principle of the DU method is to identify drugs that are widely prescribed or used (Weber et al., 2014). It is crucial to assess the usage of antihypertensive medications in order to improve the efficacy and safety of drug use in order to reach ideal blood pressure (Muliani et al., 2021). This is due to the rise in cases of hypertension as well as the

complications that might arise if hypertension is not treated effectively. Previous research results show that the antihypertensives that are widely used in one District Hospital are captopril, furosemide, nifedipine, and amlodipine. Meanwhile, the few antihypertensives used were hydrochlorothiazide, lisinopril, and bisoprolol.

METHOD

This study employs a cross-sectional design and a descriptive kind of research to evaluate the usage of antihypertensive medications. Variable data are collected to calculate the amount of antihypertensive medication use in units of DDD/100 patient days. All the components that will be researched are included in the population. All hospitalized hypertension patients made up the study's population. Purposive sampling utilizing systematic random sampling i.e., random and systematic sampling employing multiples of two for each sample to achieve 100 samples is the sampling technique used in this study. Retrospective research, or research based on patient medical records, was used to acquire the data for this study. Carrying out verification of medical record data and patterns of prescribing hypertension treatment therapy, followed by transcripts of the collected data into logbooks and computers. Data analysis carried out using the Microsoft Excel program will be analyzed using univariate analysis and the DDD/ATC method. Univariate analysis is an analysis used to analyze each variable (dependent and independent) that will be researched descriptively. Data that has been categorized is displayed as the frequency of occurrence. The DDD approach, which was processed using a combination of the Microsoft Excel application, was used to determine the amount of antihypertensive usage in hypertension patients.

RESULTS AND DISCUSSION

Based on research results, hypertension sufferers begin to occur at the age of 27 to 75 years and above, and most often occur around the age of 40 years and above. This is almost similar to the 2013 RISKESDAS data, where there was an increase in hypertensive patients aged 35–44, namely 25%. Additionally, the findings of this study are nearly in line with those of earlier research, which revealed that patients under 40 years old made up a bigger percentage of hypertension cases (39%) than patients over 40 years old (8%). Your blood pressure will rise as you become older. Collagen begins to accumulate in the smooth muscle layers of blood vessels beyond the age of 45, thickening the arterial walls. The blood vessels then gradually narrow and stiffen, raising systolic blood pressure. Age-related physiological changes include an increase in sympathetic activity and peripheral resistance. Old age causes the baroreceptor reflex, which controls blood pressure, to become less sensitive. Kidney function also declines, which lowers renal blood flow and glomerular filtration rate. According to the study's findings, there are more female hypertension patients than male patients. Female hypertension patients were higher, namely 29%, while in men it was 23%. In addition, hypertension was one of the 10 diseases with the most hospitalizations in 2020, with a case proportion of 42% of men and 58% of women, and 5% of patients died.

The impact of sex variations on blood pressure control may be related to the role played by sex hormones on the renin-angiotensin system in controlling blood pressure and cardiovascular function. Although the precise mechanism by which these sex hormones affect the control of blood pressure and cardiovascular function is still unknown, mounting evidence points to modulation of the activity of locally active hormonal systems as one of the primary mechanisms of sex hormone action on target organs, such as blood vessels and kidneys. The sex hormones estrogen and androgen play a role in the emergence of hypertension and cardiovascular disease. In general, estrogen serves to prevent, whereas androgen encourages the development of hypertension and cardiovascular disease. Estrogen, which helps to raise levels of high-density lipoprotein (HDL), protects women who haven't gone through menopause. A preventive factor in preventing the development of atherosclerosis is high HDL cholesterol levels. Premenopausal female immunity is assumed to exist because of estrogen's protective effects. Women in premenopause start to gradually lose the hormone estrogen, which shields blood vessels from harm. This process continues when the amount of estrogen in a woman's body varies naturally with age, which typically starts to happen in women over 45.

Apart from hypertension and other complications, patients also experience comorbidities. The comorbidities experienced by patients in this study consisted of cardiovascular system disorders such as stroke, heart failure, aortic aneurysm, kidney failure, and diabetes mellitus. From the results

obtained, the most common comorbidity suffered was ischemic stroke at 40%. This is different from previous research, which stated that the most common comorbidities were diabetes mellitus in 72 patients, followed by stroke in 8 patients. However, based on research conducted on more than six hundred patients who had a stroke, 59% had a history of hypertension. Patients who have a history of hypertension are at a higher risk than patients without a history of the condition. The higher the patient's blood pressure, the greater the chance of stroke, because hypertension can accelerate the hardening of the arterial walls and result in the destruction of fat in smooth muscle cells, thereby accelerating the atherosclerosis process. Hypertension plays a role in the atherosclerosis process through its suppressive effect on the endothelial cells and inner lining of the artery walls, which results in the formation of blood vessel plaque at an accelerated rate. According to research findings, stage two hypertension, defined as systolic blood pressure less than 160 and diastolic blood pressure less than 100 mmHg, affects the majority of hypertensive patients. For the purpose of treating patients, this elevated blood pressure might serve as a benchmark. The main goal of treating hypertension is to reduce mortality and morbidity associated with cardiovascular disease risk factors. The target blood pressure values for hypertensive patients recommended in JNC VIII vary based on disease complications and the race of the hypertensive sufferer. The choice of hypertension medication depends on the high blood pressure and the presence of special indications. In most patients, the desired diastolic blood pressure will be achieved when the desired systolic blood pressure has been achieved. Due to the fact that systolic blood pressure is related to cardiovascular risk compared to diastolic blood pressure, systolic blood pressure should be used as the main clinical marker for disease control in hypertension.

To determine the medications that hypertensive patients utilize, drug use patterns are distributed. According to the study's findings, up to 75% more individuals underwent antihypertensive combination therapy, or treatment for hypertension with multiple medications. According to the hypothesis, patients with stage 2 hypertension are encouraged to undertake combination therapy, which involves taking two or more medications. It is important to keep in mind while choosing antihypertensive medications that in addition to decreasing blood pressure, they can also maintain blood pressure optimally. To do this, choose between monotherapy and combination therapy for your treatment. The most popular combination therapy, however, combines CCB and ACEI, two antihypertensive medications. For stage 1 hypertension with low or moderate overall cardiovascular risk factors, monotherapy may be used as the first line of treatment. The initial dose may be increased to the maximum dose if the blood pressure target is not met. Additionally, a medicine with a different mechanism of action can be substituted for the blood pressure target if it has not been met by starting with a low dose and gradually raising it to the maximum amount. 2-3 different types of medication can be added if the intended objective is still not reached. Stage two hypertension with high or very high risk factors is treated first with a combination therapy of two low-dose medications. If with two types of drugs the target blood pressure cannot be achieved, three types of anti-hypertension drugs can be given.

From patient medical record data, data obtained includes medical record number, length of patient stay, gender, patient age, and use of antihypertensives consisting of trade name and generic name, route of administration, strength/dose, frequency, number of days of use, and amount of antihypertensive use. The dosage forms for antihypertensives, both oral and parenteral dosage forms, have the same defined daily dose (DDD) value. There are 14 types of antihypertensive drugs from six antihypertensive groups used in patients, namely ACE inhibitors, CCBs, diuretics, ARBs, beta blockers, and central two agonists. Following the calculation guidelines set by the WHO Collaborating Center in 2011, the quantity of antihypertensive usage is then determined from the data that has been obtained. Antihypertensives are categorized by ATC code and class, and the dose form is then changed to correspond to each antihypertensive's specific DDD unit. The antihypertensive dose unit must first be translated to milligrams because it is the unit used by the final DDD. The DDD value is obtained by calculating the total use of antihypertensives divided by the definitive DDD value determined by the WHO Collaborating Center based on each type of antihypertensive. Definitive DDD means one strength per patient. From the definitive DDD, the DDD usage is obtained by dividing the total usage of an antihypertensive in milligrams by the definitive DDD mg/patient. Following the acquisition of DDD usage, DDD/100 patient days is computed. DDD/100 patient days is computed by dividing the

annual total of DDD usage by the annual total of inpatient care days, which has already been divided by 100 patient days.

According to the study's findings, 100 patients required a total of 600 days of inpatient care. The total LOS used in this study was used in the DDD calculation as a divider based on the WHO DDD standard value. Based on the formulation of the DDD method, the LOS value is inversely proportional to the DDD value that will be obtained. The DDD value obtained will be smaller if the total LOS value is greater. However, the large LOS value does not always mean that the DDD value will be smaller and in accordance with the standard. Basically, DDD is a method for converting and standardizing product quantity data into rough estimates of drug use in the clinic and does not reflect actual drug use. The drug with the highest quantity of antihypertensive use is amlodipine. The DDD calculation for amlodipine reached 89 DDD/100 patient days. This indicates that 89 individuals out of the total number of study participants took 1 DDD amlodipine tablet, 5 mg, daily. A dihydropyridine CCB group is what amlodipine is. Patients with geriatric systolic hypertension take CCB medications. In a placebo-controlled trial, Systolic Hypertension Europe found that long-acting dihydropyridine CCBs significantly decreased the risk of cardiovascular events in patients with systolic hypertension. Based on the results of a systematic review of 13 guidelines for hypertension treatment therapy, JNC 8 is included in the guidelines that can be trusted for treating hypertension. Long-acting dihydropyridine (CCB), according to JNC 8, is the first-line medication for treating hypertension in older people. By blocking voltage-sensitive calcium channels and lowering the flow of extracellular calcium into cells, CCB relaxes smooth and cardiac muscles. Vasodilation is brought on by vascular muscle relaxation, which also lowers blood pressure.

Dihydropyridines (amlodipine and nifedipine) and non-dihydropyridines (verapamil and diltiazem) are two groups of CCBs. Non-dihydropyridines delay atrioventricular conduction and produce supraventricular tachyarrhythmias by inhibiting calcium channels in the heart and vasculature. Patients who suffer from angina and consequences of heart disease are prescribed diltiazem (non-dihydropyridine). Meanwhile, dihydropyridine works by stimulating baroreceptors, causing reflex tachycardia because it has a strong peripheral vasodilation effect. Dihydropyridines don't affect atrioventricular node conduction, hence they don't result in supraventricular tachyarrhythmias. Compared to cardiac calcium channels, vascular calcium channels are more responsive to dihydropyridines. Amlodipine has a greater effect on blood vessel vasodilation because these channels are more depolarized than the cardiac vascular muscle. According to the Syst-Eur trial's findings, long-acting dihydropyridine CCB medication was 42% successful in treating stroke, 26% effective in treating coronary heart disease, and 29% effective in treating heart failure. The study's findings indicated that long-acting dihydropyridine CCBs plus thiazide diuretics reduced cardiovascular morbidity and death in older adults with systolic hypertension.

Ramipril, an antihypertensive, had the second-highest usage rate, with 63 DDD/100 patient days. Angiotensin converting enzyme (ACE), which is normally responsible for activating angiotensin I to become angiotensin II, is inhibited by ramipril, a medication belonging to the ACE inhibitor class. Strong vasoconstrictor angiotensin II has the potential to increase aldosterone secretion. Additionally, ACE inhibitors prevent bradykinin from degrading and promote the production of additional vasodilators including prostacyclin and prostaglandin E2. Elevated bradykinin can amplify how well ACE inhibitors control blood pressure, but it can also bring on a dry cough as a side effect. The three ACE inhibitors ramipril, captopril, and lisinopril are the most often used ones. When compared to captopril and lisinopril, ramipril is the drug most frequently used. This distinction is based on the rationale behind selecting one of the three pharmacological classes, depending on the clinical state of the patient. Five different types of antihypertensives with long-term efficacy and safety were compared on the basis of the findings of extensive research to evaluate the effectiveness and safety of the ACE inhibitor class. Captopril, enalapril, lisinopril, ramipril, andtrandopril are the five different forms of ACE inhibitor antihypertensives. Ramipril, one of the five antihypertensives, can lower mortality in individuals with cardiovascular disease who do not have left ventricular dysfunction as well as in those who are at high risk for developing diabetes. Irbesartan had the next-highest antihypertensive usage rate (20 DDD/100 patient days). Angiotensin II type 1 (AT1) receptors, which can result in vasoconstriction, the release of aldosterone, sympathetic activity, the release of antidiuretic hormone, and the constriction and narrowing of efferent arterioles from the glomerulus, are blocked by the ARB medicine irbesartan.

Drug Utilization (DU): 90% is calculated by dividing the total antihypertensive dose per 100 patient days by the total antihypertensive dose per 100 patient days, and then multiplying the result by 100%. Following that, the percentage of antihypertensive use was totaled and ranked from highest to lowest. Drugs that are included in the cumulative 90% consumption are also included in the 90% DU section. Antihypertensive medications from the CCB group, ACE inhibitor group, and ARB group (irbesartan 9%) are all included in the DU segment. Furosemide (6%), candesartan (3%), bisoprolol (1.7%), lisinopril (2%), nifedipine (1%), clonidine (0.7%), spironolactone (0.4%), valsartan (0.2%), nimodipine (0.1%), and nicardipine (0.03%) are among the medications in the DU10% group. The findings of this study are in contrast to those of earlier studies, which revealed that in geriatric patients (60 years and over) at this District Hospital in 2011, the antihypertensive medications most commonly used were captopril (61%), furosemide (11.3%), amlodipine (8.2%), nifedipine (9.5%), hydrochlorothiazide (6%), lisinopril (3%), and bisoprolol (1%). Captopril, furosemide, and amlodipine are medications that are a part of the 90% DU category. This is due to the fact that each hospital's formulary is unique. The Pharmacy and Therapeutics Committee, which is made up of multiple doctors and pharmacists, compiles a list of the medications the hospital uses called the formulary. Because drug procurement will be more transparent thanks to the hospital formulary, hospital management will be more efficient. So that they may provide drug therapy based on what is available in the hospital, doctors use the formulary as a reference. Keep in mind that it has both a medical and an economic aspect.

CONCLUSION

Based on age and gender, hypertension patients are dominated by women. Based on the type of comorbidity, ischemic stroke is the biggest comorbidity experienced by hypertensive patients. Most hypertension patients have systolic blood pressure of less than 160 mmHg and often have diastolic blood pressure of less than 100 mmHg. According to the number of usage, it was discovered that amlodipine, with 89 DDD/100 patient days, was the antihypertensive most frequently used in hypertension patients. Amlodipine, ramipril, captopril, and irbesartan are the antihypertensive medications included in the 90% DU group, according to the DU profile. Antihypertensive medications are used in accordance with the hospital formulary. To learn more about the care patients receive, research needs to be conducted utilizing prospective methodologies and optimizing evaluation by speaking with patients, physicians, and pharmacists. It is possible to study the use of various medications using the ATC/DDD method, particularly for medications that are thought to be often used irrationally, taken by high-risk patients, have serious adverse effects, and have a limited therapeutic index.

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