EVALUATING ANTI-HYPERTENSIVE DRUGS’ SUITABILITY BASED ON THE HOSPITAL FORMULARY IN THE HOSPITAL’S PHARMACEUTICAL INSTALLATION

Retno Fitriati*, Chusun
Pharmacy Academy of Bhumi Husada Jakarta, East Jakarta, DKI Jakarta, Indonesia
* retnokartikadewi@gmail.com

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ABSTRACT

Background: Hypertension is a disease characterized by an increase in blood pressure > 140/90 mmHg. Hypertension patients usually seek treatment using a BPJS card. Medications used for BPJS patients must be in accordance with the established Hospital Formulary.

Aim: This study aims to determine the suitability of the use of anti-hypertension drugs based on the Hospital’s Formulary and the Hypertension Therapy Algorithm.

Method: This research is a descriptive study with data collection retrospectively with the research instrument being a prescription for hypertension patients. The population in this study was the prescription of Anti-Hypertension drugs in the RS. Jantung Diagram Siloam Cinere – Depok in the period August to October 2015.

Findings: From the results of the study there were 50,816 samples of anti-hypertensive drugs for 3 months consisting of August 16,807 drugs, September 16,322 drugs, and October 17687. From these data obtained all patients get a prescription in accordance with Formulary Hospital. Based on the results of the study, it can be concluded that patients who get a prescription according to the Hospital Formulary as much as 100%. From the study results, the authors suggest that doctors of the Siloam Cinere Heart Hospital Depok Depok prescribe Antihypertensive drugs in accordance with the established Hospital Formulary.

KEYWORDS conformity evaluation, anti-hypertension drugs, hospital formulary

INTRODUCTION

Health is one of the indicators of the level of human well-being so it becomes a priority in the national development of a nation (Setyaningrum, Trisiana, & Kirana, 2021). One of the most strategic components of health is the availability of drugs as part of health services to the community. The availability of adequate amounts of drugs is an important factor in national development, especially in the field of health (Satriawan, Pitoyo, & Giarisih, 2021).

Hospitals are one of the public health service facilities that play an important role in improving the degree of public health (Marnah, Husaini, & Ilmi, 2016). According to the Regulation of the Minister of Health of the Republic of Indonesia Number 58 of 2014 concerning Standards of Pharmaceutical Services in Hospitals, the definition of a Hospital is a health service institution that provides individual health services in a complete manner that provides inpatient, outpatient, and emergency services (Indonesia’s Ministry of Health, 2014).

Hypertension needs to be watched out for because it is a silent killer where symptoms can vary in each individual and are almost the same as other diseases (Kalehoff & Oparil, 2020). The symptoms are headaches or heavy feelings at the nape of the neck, vertigo, heart
Evaluating Anti-Hypertensive Drugs’ Suitability Based on the Hospital Formulary in the Hospital’s Pharmaceutical Installation

palpitations, fatigue, blurred vision, ringing of the ears, and nosebleeds (Indonesia’s Ministry of Health, 2013a).

Hypertension or high blood pressure is an increase in systolic blood pressure of more than 140 mmHg and diastolic blood pressure of more than 90 mmHg. Increased blood pressure that lasts for a long time can cause damage to the kidneys (Kidney failure), heart (Coronary heart disease), and brain (Causing stroke) if not detected early and get adequate treatment (Indonesia’s Ministry of Health, 2013b).

Hypertension is one of the leading causes of mortality and morbidity in Indonesia (Zaenurrohmah & Rachmayanti, 2017). According to basic health research 2013, people with hypertension in Indonesia at the age of ≥18 years is 25.8% while according to Riskesdas Banten, the data of people with hypertension, especially in Tangerang City has a fairly high number of 24.5%. However, diagnosed by health workers and/or a history of taking medication is only 9.5%. This indicates that most cases of hypertension in the community have not been diagnosed and affordable health services (Indonesia’s Ministry of Health, 2013b).

Rational use of antihypertensive drugs will be able to lower blood pressure with minimal toxicity risk in most patients. It should be remembered that hypertension is expressed based on blood pressure measurements not on symptoms (Hasanudin, Ardiyani, & Perwiraningtyas, 2018).

Treatment or management of hypertension takes a long time, a lifetime, and is continuous (Indonesia’s Ministry of Health, 2012). Hypertension can be prevented with a healthy lifestyle and controlling risk factors, such as regulating diet, regular exercise, avoiding smoking and alcoholic beverages, and checking blood pressure regularly (Indonesia’s Ministry of Health, 2012).

Healthy People 2010 for Hypertension advocates the need for a more comprehensive and intensive approach to achieving optimal blood pressure control. Therefore, to achieve this goal, it is necessary to actively participate with pharmacist colleagues in carrying out their professional practices in every place of health services. Pharmacists can work with doctors in educating patients about hypertension, monitoring patient responses through community pharmacy, adherence to drug and non-drug therapies, detecting and reducing side effects, and preventing and/or solving problems related to drug administration (Indonesia’s Ministry of Health, 2006). In addition, pharmacists, especially those in hospitals, can perform clinical pharmacy services in accordance with pharmaceutical service standards in hospitals. One of the clinical pharmacy services that can be done is the evaluation of drug use (Indonesia’s Ministry of Health, 2014).

This study aims to evaluate the suitability of the use of antihypertensive drugs with hospital formulary for outpatients in Internal Poly and Poly Cardiac at Siloam Diagram Heart Hospital Pharmaceutical Installation Period August-October 2015. It is hoped that this study can provide more information and contribute to the field of health, especially heart health which is undoubtedly very crucial.

METHOD

This study uses a descriptive type of research that is by evaluating the use of antihypertensive drugs, with a cross-sectional design that is the collection of variable data to find out the quantity of use of antihypertensive drugs by taking data on previous prescriptions
in Internal Poly and Cardiac Poly at Siloam Diagram Heart Hospital Outpatient Pharmacy Installation.

Data collection was carried out at Siloam Diagram Heart Hospital Outpatient Pharmacy Installation from August to October 2015. Therefore, data sources based on prescriptions from Outpatients Internal Poly and Cardiac Poly served at the Siloam Diagram Heart Hospital Pharmaceutical Installation for the period August-October 2015.

The data collected in this study was carried out by retrospective methods, namely research based on patient medical records in the form of:

1) Antihypertensive name;
2) Dosage form, dosage, the strength of the preparation, route of use, and rules of use;
3) The number of antihypertensive drugs prescribed.

Data collection and collection is carried out by collecting prescriptions of Poly Internist and Poly Cardiac to sort out the use of antihypertensive drugs for the period August-October 2015 at the Siloam Diagram Heart Hospital Outpatient Pharmacy Installation:

1) Collected data from Poly Internist and Heart prescriptions for the period August-October 2015;
2) Grouping the class of antihypertensive drugs in August-October that are included in formulary and non-formulary;
3) Calculate the highest number of antihypertensive drug use based on Formularium and Non-Formulary and present the results of observations in the form of tables and graphs;
4) Grouping the prescribing of antihypertensive drugs according to Formulary and Non-Formulary and presenting observational data in the form of tables and graphs;
5) Performs the calculation of the percentage of use of antihypertensive drugs according to Formulary and Non-Formulary and presents observational data in the form of tables and graphs;
6) Conduct discussions and conclusions from observations.

Data analysis is done using Microsoft Excel 2007, by editing data, coding data, data entry, and cleaning data. The analysis was carried out to calculate the quantity of antihypertensive use in hypertensive patients.

RESULTS AND DISCUSSION

Distribution of The Amount of Use of Antihypertensive Drugs

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Amount of Use of Antihypertensive Drugs (Tab)</th>
<th>Average/Month</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bisoprolol 5mg</td>
<td>2780 Aug, 3265 Sept, 3784 Oct</td>
<td>3276,3</td>
<td>19,21%</td>
</tr>
<tr>
<td>Candesartan 8mg</td>
<td>3442 Aug, 1788 Sept, 2407 Oct</td>
<td>2545,6</td>
<td>14,93%</td>
</tr>
</tbody>
</table>
From the results of the study, there were 50,816 samples of antihypertensive drugs for 3 months consisting of August 16,807 drugs, September 16,322 drugs, and October 17687 drugs that were evaluated for suitability of antihypertensive drugs. Based on the Hospital Formulary and Hypertension Therapy Algorithm, which can be seen in figure 1.

**Figure 1.** Distribution of Patterns of Use of Antihypertensive drugs based on Types of Hypertension drugs in Siloam Diagram Heart Hospital
Suitability of Antihypertensive Drug Use with Hospital Formulary

The overall use of antihypertensive drugs in outpatient hypertension patients at Siloam Diagram Heart Hospital compared to the Hospital Formulary. Table 4 shows that the use of antihypertensive drugs is in accordance with the Hospital Formulary with conformity of up to 100%.

Table 4. Suitability of The Use of Antihypertensive Drugs with Hospital Formulary at Siloam Diagram Heart Hospital

<table>
<thead>
<tr>
<th>Groups</th>
<th>Generic Name</th>
<th>Dosage</th>
<th>Compliance with the RS Formulary</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE Inhibitor</td>
<td>Captopril</td>
<td>Tablet</td>
<td>√</td>
</tr>
<tr>
<td></td>
<td>Lisinopril</td>
<td>Tablet</td>
<td>√</td>
</tr>
<tr>
<td></td>
<td>Ramipril</td>
<td>Tablet</td>
<td>√</td>
</tr>
<tr>
<td>b-blocker</td>
<td>Bisoprolol</td>
<td>Membrane coating tablets</td>
<td>√</td>
</tr>
<tr>
<td>Calcium Channel Blocker</td>
<td>Amlodipine</td>
<td>Tablet</td>
<td>√</td>
</tr>
<tr>
<td></td>
<td>Nicardipine</td>
<td>Injection</td>
<td>√</td>
</tr>
<tr>
<td></td>
<td>Nifedipine</td>
<td>Tablet, oros</td>
<td>√</td>
</tr>
<tr>
<td></td>
<td>Nimodipine</td>
<td>Injection</td>
<td>√</td>
</tr>
<tr>
<td>Angiotensin Receptor Blocker</td>
<td>Valsartan</td>
<td>Tablet</td>
<td>√</td>
</tr>
<tr>
<td></td>
<td>Candesartan</td>
<td>Tablet</td>
<td>√</td>
</tr>
<tr>
<td></td>
<td>Irbesartan</td>
<td>Tablet</td>
<td>√</td>
</tr>
<tr>
<td>Diuretic</td>
<td>Furosemide</td>
<td>Tablets, injections</td>
<td>√</td>
</tr>
<tr>
<td></td>
<td>Spironolactone</td>
<td>Tablet</td>
<td>√</td>
</tr>
<tr>
<td>Central a2 Agonist</td>
<td>Clonidine HCL</td>
<td>Tablet</td>
<td>√</td>
</tr>
</tbody>
</table>

% Conformity 100%

Use of Antihypertensive Drugs at Siloam Diagram Heart Hospital in August-October of 2015

The results of research conducted by researchers at the Siloam Heart Diagram Hospital obtained data on the use of the most antihypertensive drugs, namely as found in table 5.
Table 5. Use of Antihypertensive Drugs at Siloam Diagram Heart Hospital in August-October of 2015

<table>
<thead>
<tr>
<th>No</th>
<th>Antihypertensive</th>
<th>Usage (%)</th>
<th>DU segment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Amlodipine</td>
<td>40.27</td>
<td>90%</td>
</tr>
<tr>
<td>2</td>
<td>Ramipril</td>
<td>28.57</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Irbesartan</td>
<td>9.01</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Captopril</td>
<td>7.89</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Furosemide</td>
<td>5.65</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Candesartan</td>
<td>2.65</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Bisoprolol</td>
<td>1.72</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Lisinopril</td>
<td>1.70</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Nifedipine</td>
<td>1.12</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Clonidine</td>
<td>0.67</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>Spironolactone</td>
<td>0.43</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>Valsartan</td>
<td>0.22</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>Nimodipine</td>
<td>0.09</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>Nicardipine</td>
<td>0.03</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Sum</strong></td>
<td><strong>100.00</strong></td>
<td></td>
</tr>
</tbody>
</table>

From the data in table 5. It shows that antihypertensive drugs that are widely used are 90% of the Calcium Channel Blocker group (amlodipin 40.27%), ACE inhibitors (ramipril 28.57%, captopril 7.89%), ARB group (9.01%). While the less used 10% are furosemide 5.65%, candesartan (2.65%), bisoprolol (1.72%), lisinopril (1.70%), nifedipine (1.12%), clonidine (0.67%), spironolactone (0.43%), valsartan (0.22%), nimodipine (0.09%), and nicardipine (0.03%).

Discussion

The distribution of drug usage patterns aims to find out what drugs are used by hypertensive patients at Siloam Diagram Heart Hospital. Based on the results of the study, shows that patients get more antihypertensive therapy than one drug, namely antihypertensive combination therapy as much as 78%. This is in accordance with the theory that states that in patients with stage 2 hypertension it is recommended to use a combination therapy of 2 or more drugs (Ministry of Health, 2006).

The selection of antihypertensive drugs needs to be considered in addition to lowering blood pressure can also maintain blood pressure optimally (Dasgupta et al., 2014). This can be done by selecting treatment with monotherapy or combination therapy. The most antihypertensive used as monotherapy by the subjects of this study were calcium channel blockers. The most widely used combination therapy is combination therapy with 2 antihypertensive drugs, namely the Calcium Channel Blocker + ACE Inhibitor group.

According to JNC VIII, monotherapy can be given as initial therapy for stage 1 hypertension with low or moderate/moderate cardiovascular total risk factors, starting with the initial dose can then be raised to the maximum dose if the blood pressure target has not been
Evaluating Anti-Hypertensive Drugs’ Suitability Based on the Hospital Formulary in the Hospital’s Pharmaceutical Installation

reached. Furthermore, if the blood pressure target has not been reached, it can be replaced with a drug that has a different mechanism of action, starting with a low dose, and then the dose is increased to the maximum dose. If it is still not achieved the desired target can be added 2 to 3 kinds of drugs. Combination therapy 2 low-dose drugs are given for initials therapy in stage 2 hypertension with high or very high-risk factors, if 2 kinds of blood pressure target drugs are not achieved can be given 3 kinds of antihypertensive drugs.

The quantity of antihypertensive use in Siloam Diagram Heart Hospital is shown in table 5. The quantity of antihypertensive use that had the highest amount in 2015 was amlodipine. Calculations for amlodipine in 2015 mean that there were 89 patients from all study subjects who took amlodipine at 5 mg daily.

Amlodipin is a group of Calcium Channel Blocker dihydrodropiridin. Calcium Channel Blocker is used in elderly systolic hypertension patients (DiPiro et al., 2008). Systolic Hypertension–Europe conducted a trial on a controlled placebo that showed that the long-acting Calcium Channel Blocker dihydropyridine reduced the risk of cardiovascular events significantly in systolic hypertension. Calcium Channel Blockers cause relaxation of the heart and smooth muscles by inhibiting voltage-sensitive calcium channels, thereby reducing the entry of extracellular calcium into cells. Relaxation of the vascular muscles causes vasodilation and is associated with blood pressure reduction (DiPiro et al., 2008).

There are 2 classes of Calcium Channel Blockers namely dihydrodropiridin (amlodipine and nifedipine) and non-dihydrodropiridin (verapamil, diltiazem). Non-dihydrodropiridin works by blocking calcium channels in both the heart and vascular. Diltiazem (non-dihydropiridin) is used in patients with complications of heart disease and angina (Isik, Delibasi, Berker, Aydin, & Guler, 2009).

The antihypertensive with the second largest percentage of use is ramipril. Ramipril is an ACE inhibitor class drug that works by inhibiting angiotensin-converting enzyme (ACE) which under normal circumstances is in charge of activating angiotensin I into angiotensin II (Qian et al., 2019). ACE inhibitors also inhibit bradykinin degradation and stimulate the synthesis of other vasodilator substances such as prostaglandin E2 and prostacyclin (Baxter & Ebrahim, 2002). Increased bradykinin may increase the blood-pressure-lowering effects of ACE inhibitors but also cause side effects of dry cough (DiPiro et al., 2008).

There are 3 ACE inhibitors commonly used, namely ramipril, captopril, and lisinopril. The use of ramipril is the highest compared to captopril and lisinopril. The next most common use of antihypertension is irbesartan. Irbesartan is an ARB class drug that works by blocking angiotensin II type 1 (AT1) receptors that can cause vasoconstriction, aldosterone release, sympathetic activation, the release of antidiuretic hormones, and efferent renal constriction and constriction of the glomerulus (DiPiro et al., 2008).

<table>
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<td>9,01</td>
<td></td>
</tr>
</tbody>
</table>

Table 5. Use of Antihypertensive Drugs at Siloam Diagram Heart Hospital in August-October of 2015
From the data in table 5. Showed that antihypertensive drugs that are widely used are 90% of the CCB group (amlodipine 40.27%), ace inhibitor group (ramipril 28.57%, captopril 7.89%), ARB group (9.01% increase). The less used 10% are furosemid 5.65%, candesartan (2.65%), bisoprolol (1.72%), lisinopril (1.70%), nifedipin (1.12%), clonidin (0.67%), spironolactone (0.43%), valsartan (0.22%), nimodipin (0.09%), and nicardipin (0.03%).

The results of this study are different from the results of research conducted by Ivonia, et al., 2015 which showed that antihypertensive drugs used in geriatric patients (60 years and above) at Karanganyar Hospital in 2011 were captopril (60.69%), furosemide (11.26%), amlodipine (8.17%), nifedipine (9.45%), hydrochlorothiazide (5.94%), lisinopril (3.44%), bisoprolol (1.05%), and widely used drugs 90% are captopril, furosemide, and amlodipine. This is because the formulary used by each hospital is different.

A formulary is a list of drugs used by hospitals, compiled by the Pharmaceutical and Therapeutics Committee consisting of several doctors and pharmacists (Matlala, Gous, Godman, & Meyer, 2017). The formulary of the hospital will make the management of the hospital more effective, because the procurement of drugs becomes clear, considering that in addition to having the medical aspect side also has an economical side so that the formulary is used as a guide by doctors in providing drug therapy in accordance with those available in the hospital (Allerberger et al., 2016; Economou, Kaitelidou, Kentikelenis, Maresso, & Sissouras, 2015).

According to hypertension governance guidelines compiled by the Indonesian Association of Cardiovascular Specialists (PERKI) states that first-line therapy in adult hypertension patients ≥18 years old with blood pressure ≥140/90 mmHg is a lifestyle modification to control their blood pressure. If the blood pressure target has not been achieved, pharmacological therapy is starting to be given, especially in patients with stage 2 hypertension and patients who have complications. In stage 1 patients the selection of therapy is distinguished again based on age, if the patient is <60 years old the first-line therapy given is ACEI or ARB and if the patient is ≥60 years old then the first-line therapy is CCB or Tiazid. While in stage 2 patients, you should start with a combination of two drugs. The combination therapy that can be given is CCB or Tiazid in combination with ACEI or ARB.
Evaluating Anti-Hypertensive Drugs’ Suitability Based on the Hospital Formulary in the Hospital’s Pharmaceutical Installation

The Role of Pharmacists in Hospitals

Based on the Regulation of the Minister of Health No. 58 concerning Pharmaceutical Service Standards in Hospitals, it is stated that the role of Pharmacists in Hospitals is one of them is to perform Clinical Pharmacy Services. Clinical pharmacy services are direct services provided by pharmacists to patients in order to improve therapeutic outcomes and minimize the risk of side effects due to drugs, for patient safety purposes so that patient quality of life (quality of life) is guaranteed (Indonesia’s Ministry of Health, 2014).

Clinical pharmacy services carried out include assessment and prescription services, tracing drug use history, drug reconciliation, Drug Information Services (PIO), counseling, visite, Drug Therapy Monitoring (PTO), Drug Side Effects Monitoring (MESO), Drug Use Evaluation (EPO), sterile preparation dispensing, and Monitoring of Drug Levels in the Blood (PKOD).

One of the clinical pharmacy services that can be done is drug use evaluation (EPO). EPO is a program that is structured and continuous qualitatively and quantitatively. The purpose of EPO is to get an overview of the current state of drug use patterns, compare drug use patterns in a certain period of time, provide input for improvements in drug use, and assess the influence of interventions on drug use patterns (Indonesia’s Ministry of Health, 2014).

Evaluation of drug use is very important to be done by pharmacists because it can guarantee the accuracy of prescribing and use of drugs, is cost-effective, and can improve the quality of health services so as to determine the basis of rational treatment. The results of subsequent assessments become the basis for identifying shortcomings and strategizing for improvement. When a problem is identified, an intervention is designed and applied to correct the pattern of drug use. Interventions that can be carried out include educational programs, provision of drug information, changes in hospital policies and procedures, and changes in hospital formulary (WHO Int WG for Drug Statistics Methodology, 2003).

CONCLUSION

1) Based on the amount of use of antihypertensive drugs in outpatient hypertension patients at Siloam Diagram Heart Hospital compared to Hospital Formulary. Show that the use of antihypertensive drugs is in accordance with the Hospital Formulary with conformity reaching 100% in Poli Internis and poly cardiac hospitals. Siloam Diagram Heart;

2) Based on the number of uses, the most antihypertensive use was obtained in the 3rd most hypertensive patients included in the Hospital Formulary at Poli Internis and Poly Heart Hospital. Siloam diagrams are Amlodipin, Ramipril and Captopril;

3) Based on the number of uses of this type of antihypertensive drug there is no writing of antihypertensive drugs that are outside the Formulary of hospitals in Poli Internis and poly cardiac hospitals. Siloam Diagram Heart; and

4) Based on the number of uses of antihypertensive drugs, it shows that antihypertensive drugs that are widely used are 90% consisting of the Calcium Channel Blocker group (amlodipine 40.27%), ace inhibitors (ramipril 28.57%, captopril 7.89%), ARB group (9.01%). While the less used 10% are furosemid 5.65%, candesartan (2.65%), bisoprolol (1.72%), lisinopril (1.70%), nifedipin (1.12%), clonidin (0.67%),
Evaluating Anti-Hypertensive Drugs’ Suitability Based on the Hospital Formulary in the Hospital’s Pharmaceutical Installation

- spironolactone (0.43%), valsartan (0.22%), nimodipin (0.09%), and nicardipin (0.03%).

Therefore, it is necessary to conduct research using prospective methods and optimization of evaluations with interviews with patients, doctors, and pharmacists to dig deeper into information about the treatment provided to patients. In addition, it is also necessary to use the ATC / DDD method in order to research the use of other drugs, especially for drugs that are suspected to be widely used irrationally, used by high-risk patients, and have significant side effects and a narrow therapeutic index.

REFERENCES


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