

Antihypertensive Drug Use after a New Drug Formulary Implementation in a Private Hospital in Indonesia

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Abstract

There are many antihypertensive drugs available, but the drugs that have been proven to reduce cardiovascular events should be preferred. This study aims to assess antihypertensive drug prescribing after the implementation of a new drug formulary in a private hospital in Indonesia. This cross-sectional study was conducted on 345 patients with hypertension in a private hospital in Indonesia. Antihypertensive drug use data in the period after the implementation of a new drug formulary (2013-2015) were extracted from the hospital medical records. The characteristics of the prescriptions, the name and pharmacological classification of the antihypertensive drugs prescribed, types of combination antihypertensive drugs and consistency with the Indonesian National Formulary were assessed. This study included 345 hypertensive patients with 1126 prescriptions containing 3292 drugs. There were 35.4% antihypertensive drug prescriptions, with 3.6% prescriptions containing antihypertensive drug combinations. Calcium channel blockers (74.8%) were most commonly prescribed, with amlodipine as the most common drug name prescribed. A most prevalent antihypertensive drug used in combination was hydrochlorothiazide and captopril (47.5%). All antihypertensive drugs were consistent with the Indonesian National Formulary. In conclusion, The pattern of antihypertensive drug use after the implementation of an evidence-based hospital formulary showed a trend of a better and more rational use of antihypertensive drugs.

Keywords: antihypertensive drug, hypertension, formulary, generic drug

INTRODUCTION

Hypertension accounts for around 9.4 million mortality cases every year worldwide and also accounts for 45% mortality cases caused by heart diseases and 51% mortality cases caused by stroke. Around 40% adults are diagnosed with hypertension, with higher prevalence is shown in lower- and middle-income countries. Due to issues in the health system, there are many undiagnosed and untreated hypertension patients in these countries [1,2]. There was a lot of evidence showing the association between hypertension and the increase in cardiovascular disease risk [3,4]. Hypertension is one of the top causes of death and disability-adjusted life years in the world [5].

There are various factors that may contribute to the development of hypertension and its complications, including social determinants (globalization, urbanization, aging, income, education, housing) and behavioral risk factors (unhealthy diet, smoking, physical inactivity, harmful alcohol use). Together with diabetes, obesity, and dyslipidemia, hypertension is one of the risk factors for cardiovascular diseases and kidney failure. Early detection and non-pharmacological as well as pharmacological treatment of hypertension will contribute to the decrease in cardiovascular mortality. Along with the treatment of other risk factors, the approach has reduced the mortality due to heart diseases and stroke in higher-income countries [1].

The management of hypertension consists of non-pharmacological and pharmacological treatments. Non-pharmacological treatments are effective for hypertension, with the most important are weight reduction, diet, sodium reduction, potassium supplementation, increased physical activity, and reduced alcohol use. Meanwhile, the pharmacological treatment with antihypertensive drugs is recommended for secondary prevention of recurrent cardiovascular events in patients with clinical cardiovascular diseases and average systolic blood pressure of 130 mmHg or higher or an average diastolic blood pressure of 80 mmHg or higher, and for primary prevention in adults with estimated 10-year atherosclerotic cardiovascular disease risk of 10% or higher and an average systolic blood pressure 130 mmHg or higher or an average diastolic blood pressure 80 mm Hg or higher. Antihypertensive drugs are also recommended for primary prevention of cardiovascular diseases in adults with no history of cardiovascular diseases and with an estimated atherosclerotic cardiovascular disease risk < 10% and a systolic blood pressure of 140 mm or higher or a diastolic blood pressure of 90 mmHg or higher. There are many antihypertensive

drugs available, but the drugs that have been proven to reduce cardiovascular events should be preferred, which includes thiazide diuretics, angiotensin-converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), and calcium channel blockers (CCBs). There is not enough evidence on the initial use of beta-blockers for hypertension without any specific cardiovascular comorbidities [6-10].

In recent years, there has been an increase in public spending on hospital drugs, with reasons partly associated with lack of control of non-formulary prescribing and lack of fraud control. Appropriate drug use in the hospital includes the selection and formulary management by multidisciplinary committee. Hospital formulary is the core in hospital drug management [11]. Hospital formulary will facilitate the standard of best practice, ensure rational drug therapy, promote high quality evidence-based prescribing, reduce variations in the level of treatment between patients, and control drug cost [12].

A new drug formulary was implemented in a private hospital in Indonesia. This formulary is expected to stimulate a better and rational drug prescribing. This study was conducted with the objective to assess antihypertensive drug prescribing after the implementation of an evidence-based hospital formulary in a private hospital in Indonesia.

MATERIALS AND METHODS

The design of this study was cross-sectional study. Before the assessment of antihypertensive drug prescribing, an evidence-based drug formulary was developed by emphasizing on evidence-based treatment and generic formulations. The evidence-based formulary was developed after data collection and analysis in 2010-2011. Based on the data in 2010-2011, the draft for evidence-based formulary was prepared. Medical experts were invited to review the formulary draft before the implementation in the hospital healthcare. Furthermore, more data were collected 2 years after the formulary implementation, namely in 2013-2015.

Drug use data in the period after the formulary implementation (2013-2015) were extracted from the hospital medical records. Drug use after the formulary implementation in the hospital outpatient clinic was assessed. Drug use items assessed were the average numbers of antihypertensive drugs prescribed per prescription, the proportions of antihypertensive drug combinations prescribed, pharmacological classification, the name of antihypertensive drugs, type of antihypertensive

combinations, and consistency with the Indonesian National Formulary.

RESULTS

This study included 345 hypertensive patients with 1126 prescriptions containing 3292 drugs. Table 1 presents the characteristics of these patients and their prescriptions. Most patients were males (68.4%). Most drugs prescribed were generics (67.9%) given as single drugs (90.0%). Only 66.5% drugs prescribed were consistent with the National Formulary. Most prescriptions contained 3 or more drugs (70.2%). The average number of medicine per prescriptions was 2.92±0.93 per patient. From all drugs prescribed, 35.4% were antihypertensive drugs. There were only 3.6% prescriptions containing antihypertensive drug combination, while the rest contained single antihypertensive drugs.

Based on the pharmacological classification, antihypertensive drugs prescribed were mostly from calcium channel blockers class (74.8%), while the rest were agents acting on the renin-angiotensin system (20.3%), diuretics (3.2%), and beta-blocking agents (1.7%) (Table 2). Based on the Anatomical Therapeutic Chemical (ATC) code, amlodipine was prescribed the most (68.8%), followed by captopril (20.1%), and nifedipine (6.0%) (Table 3 and Figure 1). From all antihypertensive drug combinations, the combination of hydrochlorothiazide and captopril was the most common (47.5%), followed by the combination of bisoprolol and nifedipine (10.0%), amlodipine and irbesartan (7.5%), amlodipine and captopril (7.5%), bisoprolol and captopril (7.5%), and hydrochlorothiazide and nifedipine (7.5%) (Table 4)..

Compared with the Indonesian National Formulary, all of the antihypertensive drugs prescribed were consistent. Most of the drugs were prescribed as generics. Only a few antihypertensive drugs were prescribed as branded formulations, namely, 5 prescriptions of amlodipine, 4 prescriptions of captopril, 3 prescriptions of furosemide and 1 prescription of atenolol (Table 5).

Table 1. Characteristics of hypertensive patients

Characteristics	n (%)
Gender (n = 345)	
Male	236 (68.4)
Female	109 (31.6)
Generic drugs (n = 3292)	
Yes	2234 (67.9)
No	1058 (32.1)
Type of drugs (n = 3292)	
Single	2962(90.0)
Combination	330(10.0)
Consistency with Indonesian National Formulary (n = 3292)	
Yes	2188 (66.5)
No	1104 (33.5)
Number of drugs per prescription	
1	63 (5.6)
2	273 (24.2)
3	534 (47.4)
4	211 (18.7)
5 or more	45 (4.1)
Average number of medicine per prescriptions, mean (SD)	2.92 (0.93)
Antihypertensive drugs	
Yes	1167 (35.4)
No	2125 (64.6)
Antihypertensive drug prescription, mean (SD)	1.03 (0.18)
Combination antihypertensive drugs	
Combination	40 (3.6)
Single	1086 (96.4)

Table 2. Pharmacological classification of antihypertensive drugs prescribed

Pharmacological classification	n (%)
Calcium channel blockers	873 (74.8)
Agents acting on the renin-angiotensin system	237 (20.3)
Diuretics	37 (3.2)
Beta blocking agents	20 (1.7)

Table 3. The name and the Anatomical Therapeutic Chemical (ATC) code of antihypertensive drugs prescribed

Name of drug	n (%)	Percentage
Amlodipine (C08CA01)	803	68.8
Captopril (C09AA01)	234	20.1
Nifedipine (C08CA05)	70	6.0
Hydrochlorothiazide (C03AA03)	34	2.9
Bisoprolol (C07AB07)	19	1.6
Furosemide (C03CA01)	3	.3
Irbesartan (C09CA04)	3	.3
Atenolol (C07AB03)	1	.1
Total	1167	100.0

Table 4. Combination antihypertensive drugs prescribed

Combination	n (%)
Hydrochlorothiazide + captopril	19 (47.5)
Bisoprolol + nifedipin	4 (10.0)
Amlodipine + irbesartan	3 (7.5)
Amlodipine + captopril	3 (7.5)
Bisoprolol + captopril	3 (7.5)
Hydrochlorothiazide + nifedipine	3 (7.5)
Captopril + nifedipine	2 (5.0)
Amlodipine + furosemide	1 (2.5)
Amlodipine + hydrochlorothiazide	1 (2.5)
Furosemide + nifedipine	1 (2.5)

Table 5 Consistency of the antihypertensive drugs prescribed to the Indonesian National Formulary

Name of drug	National Formulary					
	Consistent			Not consistent		
	generi c	brande d	%	generi c	brande d	%
Amlodipine	798	5	68.8	0	0	0
Captopril	230	4	20.1	0	0	0
Nifedipine	70	0	6	0	0	0
Hydrochlorothiazide	34	0	2.9	0	0	0
Bisoprolol	19	0	1.6	0	0	0
Irbesartan	3	0	0.3	0	0	0
Furosemide	0	3	0.3	0	0	0
Atenolol	0	1	0.1	0	0	0

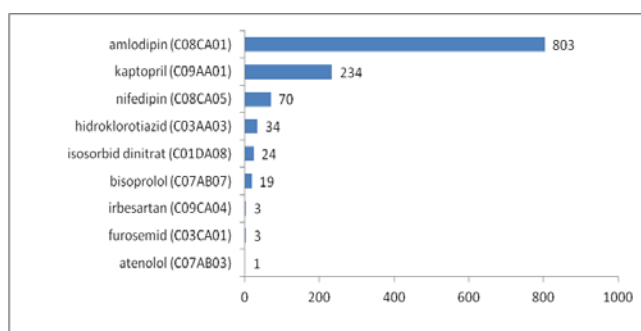


Figure 1. Proportion of antihypertensive drugs prescribed

DISCUSSION

This study gave an illustration of antihypertensive drug prescribing after the implementation of an evidence-based hospital formulary in a private hospital in Indonesia. The prescribing of antihypertensive drugs made up around a third of all drugs prescribed. Only a few antihypertensive drugs were prescribed in combination. All of the antihypertensive drugs prescribed were consistent with the Indonesian National Formulary.

Calcium channel blockers (CCBs) are the most common antihypertensive drugs prescribed (74.8%) in the private hospital in this study, followed by agents acting on the renin-angiotensin system (20.3%), diuretics (3.2%), and beta-blockers (BBs) (1.7%). The proportions are almost similar to a study conducted in the in-patients of a tertiary health care facility in Nigeria. The most common antihypertensive drugs prescribed were CCBs (70.4%), followed by angiotensin-converting enzyme inhibitors (ACEIs), diuretics, centrally acting agents, angiotensin receptor blockers (ARBs), and BBs [13]. Another similar study was conducted in 59 hospitals in China, and it showed that CCBs were the most common antihypertensive drugs used (42.8%), followed by ARBs, ACEIs, BBs, and diuretics [14]. CCBs (and BBs) were also the most commonly prescribed patients with uncomplicated hypertension in Taiwan. Despite their lower cost, diuretics were less commonly prescribed, either as monotherapy and as overall, similar to the results of our study [15]. In another study conducted on the use of antihypertensive drugs in Spanish primary health care, agents acting on the renin-angiotensin system were the most common (around 57.6%) during 1990-2012 [16]. This shows that different settings might affect the use of the most common antihypertensive drugs.

According to the treatment algorithm in the guideline that is applicable during the period the drugs prescribed (Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure/JNC 7), thiazide-type diuretic should be the initial therapy for most patients, either as a single agent or as a combination with other antihypertensive drug(s), such as angiotensin-converting enzyme inhibitor (ACEI), angiotensin receptor blocker (ARB), CCB, or BB. If one of these other antihypertensive drugs is selected as initial therapy, the reason should be either because the patient cannot use diuretics, or when there is a compelling indication that warrants the use of a specific antihypertensive drug. For example, CCB is recommended to be used in hypertensive patients with high coronary disease risk or diabetes [17]. It is possible that CCB was more commonly used in the private hospital in this study because of these two reasons.

The combination of hydrochlorothiazide and captopril was the most common combination antihypertensive drugs prescribed, followed by the combination of bisoprolol and nifedipine, amlodipine and irbesartan, amlodipine and captopril, bisoprolol and captopril, hydrochlorothiazide and nifedipine. Another study conducted in Ethiopia showed an almost similar pattern, where the most common combination prescribed was hydrochlorothiazide and enalapril [18]. A study conducted in the outpatient unit of a teaching hospital also showed that the combination of hydrochlorothiazide and ACEI or ARB is the most frequently prescribed antihypertensive combination. The combination of CCB and ACEI or ARB is also quite common (25%) [19], similar to our study with the combination of amlodipine and irbesartan as well as amlodipine and captopril.

According to the JNC 7, combination of two antihypertensive drugs is recommended for those with systolic blood pressure ≥ 160 mmHg or diastolic blood pressure of ≥ 100 mmHg, or when single drug therapy in proper dose fails to achieve blood pressure control. The combinations recommended are thiazide-type diuretics and either one of ACEI, ARB, CCB, or

BB [17]. Based on this, the populations assessed in this study might have a milder stage of hypertension or uncomplicated hypertension. Most of the choices of antihypertensive combination in our study are in agreement with this guideline. The antihypertensive drugs prescribed in this study are also consistent with the antihypertensive drugs recommended in the Indonesian National Formulary.

Based on a meta-analysis conducted to compare the effectiveness of antihypertensive drugs for primary prevention of cardiovascular diseases, BBs are less effective in reducing mortality compared to ARBs. ACEIs are less effective in reducing stroke compared to CCBs, but ACEIs are more effective in reducing heart failure compared to CCBs. Diuretics lower the risk of heart failure and myocardial infarction compared to CCBs and BBs, but diuretic users more commonly suffer from diabetes compared to ACEIs and CCBs. To sum up, every antihypertensive drug class has its own benefit, but BBs and alpha-blockers might not be the first-choice antihypertensive drugs [20-23]. In our study, BBs were the least common antihypertensive drug group prescribed, while alpha-blockers were not prescribed at all. Overall, the prescription of antihypertensive drugs after the implementation of new medicine formulary was apparently rational.

CONCLUSION

In conclusion, the pattern of use of antihypertensive drugs after the implementation of a new medicine hospital formulary showed a trend of a better and more rational use of antihypertensive drugs, as evidenced by the prescriptions of antihypertensive drugs that were consistent with the hypertension guideline and the Indonesian National Formulary.

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