

# The Incidence Side Effects of Antihypertensive Drugs in the Intensive Care Unit General Hospital Dr.M.Ddjamil Padang

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## Abstract:

To lower morbidity and mortality from disease complications, the goal of hypertension treatment is to maintain target blood pressure. The management of hypertension necessitates lifelong medication, which carries the risk of adverse drug reactions. This study attempts to ascertain the occurrence of antihypertensive drug side effects and the description of antihypertensive drug use in Dr. M. Djamil Padang Hospital's Intensive Care Unit based on the Naranjo algorithm. Using cross-sectional methodology and retrospective data, this study is an example of non-experimental descriptive research. 60 patients met the inclusion criteria according to the study's findings. The most utilized medicines were those in the Calcium channel blocker (CCB) class. The incidence of side effects was found to be 18 patients (55 different types of pharmaceuticals) in the moderately likely category and 1 patient (2 different types of drugs) in the uncertain category based on the Naranjo algorithm. The side effects that caused more than 10% were edema (12.28%), hypotension (38%), cough (15.78%), and hyponatremia (14.03%). Chest pain (8.77%), shortness of breath (5.26%), nausea, and vomiting (5.26%) were the side effects that manifested <10%. Antihypertensive medication side effects remain in the Central General Hospital (RSUP), Dr. M. Djamil Padang's Intensive Care Unit (ICU).

**Keywords:** antihypertensive drug, side effect, Naranjo

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## 1. Introduction

An abnormal rise in arterial blood pressure that lasts for longer than a few minutes is known as hypertension, or high blood pressure. When a person's blood pressure is greater than 140/90 mmHg, hypertension is diagnosed. In addition to increasing the risk of heart, brain, and renal illness, hypertension is the primary cause of premature death globally (World Health Organisation, 2021). In Indonesia, 34.1% of people have hypertension, while West Sumatra is third with 25.16% of cases occurring in people who are at least 18 years old (Kementerian Kesehatan Republik Indonesia, 2018). Patients with uncontrolled blood pressure may be more at risk for worsening heart and renal function, as well as unfavourable clinical signs such as heart failure, respiratory failure, admission to the intensive care unit (ICU), and mortality. In 2022, Mangopo *et al.* As a result, treating hypertension can lower the morbidity and death linked to high blood pressure. In addition, maintaining blood pressure vibrations is the major goal of this hypertension treatment (Adistia *et al.*, 2022).

Treatment of hypertension requires long-term treatment, even for life (Mursiany *et al.*, 2015, Pahlawan *et al.*, 2013). A drug side effect is an adverse and undesirable response of a drug to a dose normally used in humans for the prevention, treatment, or diagnosis of a disease (Badan Pengawasan Obat dan Makanan Republik Indonesia, 2012). Then the use of antihypertensive drugs should be monitored so that the patient's blood pressure is constantly controlled, which can reduce morbidity and mortality associated with hypertension and minimise the occurrence of side effects of the drug.

Patients whose blood pressure is uncontrolled independently may be at risk of adverse clinical symptoms such as respiratory failure, heart failure, Intensive Care Unit (ICU) admission, and death, as well as showing worse heart and kidney function (Mangopo *et al.*, 2022). Therefore, hypertension treatment can reduce the morbidity and mortality associated with high blood pressure. Besides, the primary purpose of this hypertension treatment is to maintain blood pressure vibrations. (Adistia *et al.*, 2022). Treatment of hypertension requires long-term, even lifelong, treatment. (Mursiany *et al.*, 2015). Long-term hypertension treatment can cause side effects of medication (Pahlawan *et al.*, 2013). A drug side effect is an adverse and undesirable response of a drug to a dose normally used in humans for the prevention, treatment, or diagnosis of a disease (Badan Pengawasan Obat dan Makanan Republik Indonesia, 2012). Then the use of antihypertensive drugs should be monitored so that the patient's blood pressure is constantly controlled, which can reduce morbidity and mortality associated with hypertension and minimize the occurrence of side effects of the drug.

Over a decade of research into the side effects of antihypertensive drugs in several hospitals and public health centre has shown that there are cases of side effects. The results of the study by Kumar *et al* (2011), showed that there were 18 cases (52.9%) of side effects in the mild category, 14 cases (41.2%) in the moderate category, and 2 cases (5.8%) in the severe category. In the study Shrestha *et al.* (2012) side effects of the drug occurred in the use of amlodipine 41%, atenolol 42,9%, and the case of side effects with the majority occurred was enalapril 73,3%. In the research of Pahlawan *et al* (2013) in the Ambulatory of Muhammadiyah Hospital Palembang, long-term use of antihypertensive medication can cause side effects such as captopril use, which can cause proteinuria. In the Kristanti (2015) study in the public health centre Kalirungkut Surabaya, the incidence of side effects of the drug captopril was 36%, and side effects on amlodipine were 46%.

These research findings indicate that both inpatient and ambulatory care patients have experienced antihypertensive medication side effects. ICU patients are also likely to experience it. Individuals receiving ICU care are in a critical state and need close observation. An area of a hospital called the ICU has specialized personnel and technology designed to monitor and treat patients with critical, life-threatening, and uncertain prognoses (Rahmanti, 2021). Therefore, the researchers would want to investigate the adverse effects of antihypertensive medications at the Central General Hospital (RSUP), Dr. M. Djamil Padang, Intensive Care Unit (ICU).

## 2. Method

This research is a type of non-experimental descriptive research with data of a retrospective nature using cross-sectional methods. Data were taken from the medical records of patients taking antihypertensive drugs at the Intensive Care Unit (ICU) of M. Djamil Padang Central General Hospital. The research was conducted from November 2022 until April 2023. Using purposive sampling procedures, the study's sample consisted of all patients in the intensive care unit (ICU) who were prescribed antihypertensive medications and satisfied the inclusion criteria. Patients taking oral antihypertensive medication and injectables, with or without concomitant conditions, and patients over the age of 18 meet the inclusion criteria. The exclusion criteria are medical records that are unreadable or incomplete.

A research instrument is a tool used by a researcher to collect data on a variable or topic under study. In this study, the following tools were utilized: To obtain data from the medical record sheet and utilize the patient data collecting form. the Naranjo scale is formed. DIH (Drug Information Handbook, 17th Edition) and Medscape.com. The independent variable are gender, age, and prescription of antihypertensive drug. The dependent variable is side effect of that medication. Data from the results of the study are analysed descriptively about the characteristics of the subject of study and the problems related to the drug studied in the form of tables and graphs.

## 3. Result and Discussion

### 3.1 Result

Under the heading "Study of Side Effects of Antihypertensive Drugs in the Intensive Care Unit of Dr. M. Djamil Padang Public Hospital," and with the ethical study number (No. LB.02.02/5.7/146/2023), the study was conducted at Dr. M. Djamil Padang's Central Public Hospital (RSUP). 60 patients met the inclusion criteria out of the 110 Intensive Care Unit (ICU) patients who received antihypertensive medication therapy at RSUP DR. M. Djamil Field from January to December 2022. In this study, 17 out of the 60 patients had pharmacological

side effects that were assessed. There were 27 men (45%) and 33 women (55%), who were getting gender-based antihypertensive medication therapy in the intensive care unit (ICU). Based on age groupings, the distribution of patients receiving antihypertensive medicine in the ICU is as follows: six patients in the early adult (10%), eighteen patients in the middle adult (30%), and thirty-six elderly patients (later adult) (60%). The drug usage profile of the patients is as follows: diuretic pharmaceuticals have a rate of 35%; beta-blockers have a proportion of 28.33%; ACE inhibitors have a ratio of 25%; calcium channel blockers (CCB) have a percentage of 66.66%; and angiotensin receptor blocker (ARB) medications have a percentage of 61.66%.

Table 1: Characteristic Patient

No	Variable	Frequency	Percentage (%)
1	Gender		
	Female	27	45
	Male	33	55
2	Age		
	26-44 yo	6	10
	45-59 yo	18	30
	>60 yo	36	60
3	Incidence side effect		
	With side effect	17	28.33
	Without side effect	43	71.66

The prescription pattern consists of calcium channel blockers (CCBs) with a percentage of 66.66% in patients; angiotensin receptor blockers (ARBs) with 61.66%; diuretic drugs with 35%; beta-blockers with 28.33%; and ACE inhibitors with 25%.

Table 2 : Side effect of antihypertensive drug

No	Side effect	Antihypertensive drug	Frequency	Percentage (%)	Scale
1	Nausea and vomiting	Bisoprolol	1	5,26	fairly possible: 1-4 poin
		Ramipril	1		
		Spirolactone	1		
2	Breathlessness	Bisoprolol	3	5,26	fairly possible: 1-4 poin
3	Chest pain	Amlodipine	3	8,77	fairly possible: 1-4 poin
		Candesartan	2		
4	Oedema	Amlodipine	4	12,28	fairly possible: 1-4 poin
		Candesartan	3		
5	Dry cough	Bisoprolol	2	15,78	fairly possible: 1-4 poin
		Candesartan	4		
		Ramipril	3		
6	Hyponatremia	Candesartan	9	14,03	fairly possible: 1-4 poin
7	Hypotensi	Amlodipine	7	38,59	fairly possible: 1-4 poin hesitation: 0-
		Bisoprolol	3		
		Candesartan	7		
		Lasic	2		
		Ramipril	3		

### 3.2 Discussion

The demographic data of ICU patients receiving antihypertensive drug therapy based on gender were 27 male patients (45%) and 33 female patients (55%). Basic Health Research (2018) showed that women were more likely to suffer from hypertension than men, with a prevalence of 36.9% in women and 31.1% in men.

This is because menopause is one of the factors that causes women to have a higher incidence rate than men because of low oestrogen levels in menopausal women. While this oestrogen works to increase the level of high-density lipoprotein (HDL), which plays a major role in the health of blood vessels (Falah, 2019), In the Intensive Care Unit (ICU) distribution of patients receiving antihypertensive drug therapy based on age categories, it indicates that the older they get, there will be structural changes in the large blood vessels, so that the lumen becomes narrower and the blood vessel walls become stiffer, which can lead to an increase in blood pressure (Taiso *et al.*, 2021).

In this study, the number of cases of side effects was 58. The side effects found in patients were then assessed using the Naranjo scale. The completion of the Naranjo algorithm is based on the medical record data obtained, such as integrated patient progress records (CPPTs) of initial physical examinations, examinations of early vital signs, patient complaints, and laboratory examinations. The Naranjo algorithm is a special instrument used by the Drug and Food Supervision Agency of the Republic of Indonesia as a reference for monitoring drug side effects in Indonesia. The purpose of using the Naranjo algorithm is to assess the association of side effects with the suspected drug. Based on the Naranjo algorithm, these side effects can be categorised as quite possible (scores 1-4). 17 patients were associated with the use of 56 types of medication, and in the category of hesitation (score 0-), as many as 1 patient was related to the use of 2 items.

Using medscape.com and the DIH (Drug Information Handbook) as guidelines, the results analysis scale Naranjo shows a quite possible category (score 1-4) for the single patient who presents in the CPPT with symptoms of nausea and vomiting while taking bisoprolol, ramipril, and spironolactone.

This study indicates that three patients with probable side effects of breathlessness related to bisoprolol medication are now enrolled in the CPPT. The patients' complaints of breathlessness on Algorithm Naranjo come into the classification considered fairly possible (scoring 1-4). Bisoprolol is a beta-blocker that can cause asthma; it also includes those regarded as cardio selective. As a result, those with a history of bronchospasm or asthma should refrain from using it (PIONAS, 2014). Because bisoprolol was an antihypertensive cardio selective beta-blocker, it produced dyspnoea in prior research. While the  $\beta_2$  adrenergic receptor is widely distributed in the bronchi, the  $\beta_1$  adrenergic receptors are mostly located in the heart tissue. The blockade of the  $\beta_2$ -adrenergic receptor causes bronchospasm or shortness of breath (Sholihah & Hanugrah, 2020).

According to the observed patients' medical records, three patients and one patient had side effect related to chest pain that was suspected to be caused by the use of candesartan and amlodipine. The three medications fell into a very reasonable category (scoring 1-4) according to the study using the orange scale. The negative effects found are based on patient complaints that have been modified or are detailed in the guidelines on Medscape.com. The results are also consistent with JNC-8, suggesting that chest pain is one of the significant side effects of amlodipine (Lusi *et al*, 2022). Chest pain, 0.1%–1% frequency of side effects on candesartan adjusted with drugs.com (rarely).

There were 4 patients with oedema recorded in the CPPT suspected of the use of amlodipine and candesartan. The results of the analysis with the Naranjo scale show quite possible categories (score 1-4). In other clinical trials, it is known that both CCB and ACEI have a positive effect on cardiovascular outcomes, so the combination of ACEIs and CCBs is rational and has high effectiveness. The most common side effect of CCB is peripheral oedema. This effect occurs due to a larger arteriolar limitation than the circulation of the veins, resulting in an increase in the transcapillary gradient and capillary leakage (Ahadiyah *et al.*, 2019).

There are six patients with cough side effects recorded in the CPPT allegedly due to the use of ramipril, candesartan, and bisoprolol, with quite possible categories (score 1-4). The results of the analysis with the Naranjo scale indicate that ACEI drugs can cause dry cough because ACE-inhibitor drugs cause bradykinin to become an active metabolite and there is an accumulation of bradykinin (Wicaksono *et al.*, 2021). The results of a study at Cengkareng Hospital showed that there was an 8.69% incidence of dry cough in patients taking ramipril. (Halim & Supardi, 2015). According to a study by Mursiany, *et al.* (2013), candesartan is an ARB group that does not cause bradykinin effects that cause the appearance of coughing side effects, such as in the use of ACEI. On the other hand, on medscape.com and drugs.com, there are cough side effects on candesartan with an unspecified frequency or that are still rare.

Eight patients were identified using data from the observed medical records. The patient's sodium levels decreased from the usual range of 135–144 mmol/L, and the medication candesartan may have caused hyponatremia side effects; this was classified as quite likely (scoring 1-4). The guidelines on this prescription,



specifically medscape.com and DIH (Drug Information Handbook), define how side effects of hyponatremia on the drug Candesartan should be changed. Additionally, drugs.com has altered these side effects with a frequency of 0.1%–1% (rarely).

Side effects of hypotension were found in clinical trials suspected of the use of candesartan, amlodipine, Lasix, bisoprolol, and ramipril. The results of the analysis with the Naranjo scale show quite possible categories (scores 1-4) and hesitate categories (scores 0-). The side effects of hypotension obtained from candesartan and amlodipine based on clinical examination of patients are based on the DIH (Drug Information Handbook) as a guideline and are adjusted on Drugs.com with the frequency of side effects from hypotension of Amlodipine 0.1%–1% and Candesartan 1%–10%.

There are several restrictions on this study, including the use of retrospective research, which limits researchers from having direct contact with patients, and using medical records as the only data source. This study is further limited by the poorly suited and sequential data recording from medical records and a small number of incomplete or missing records. Issues related to adverse drug reactions, such as adverse effects that arise right after the patient starts antihypertensive medication therapy, cannot be recognized since to do so, a direct observation and conversation with the patient are required.

#### 4. Conclusion

The following conclusions can be drawn from the study on the adverse effects of antihypertensive medications in patients receiving treatment at the Intensive Care Unit (ICU) at RSUP Dr. M. Djamil Padang: The representation of patients in the ICU on antihypertensive medicine The most often used are the calcium channel blocker (CCB) classes of medications, which include nifedipine, nicardipine, and amlodipine. The angiotensin receptor blocker (ARB) medicine class, which includes valsartan and candesartan, is the second most prevalent category of medications. The diuretics include furosemide, spironolactone, and hydrochlorothiazide; the beta-blockers are bisoprolol and propranolol. The ACE inhibitor ramipril belongs to the smallest class of medications. An overview of cases of side effects of antihypertensive drugs in patients of the Intensive Care Unit (ICU) based on the Naranjo algorithm with a category of fairly possible (score 1-4) of 17 patients (56 types of medication) and a questionable category of 1 patient (1-4 scores) (2 types of medication).

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