

Research Article

## Changes in Mean Arterial and Blood Pressure in Using Nicardipine in Hypertensive Crisis Patients at the Hajj General Hospital Surabaya from August to December 2021

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### Abstract

Hypertension crisis is one of the most common disease problems; it will cause complications and death. Therapeutic management guidelines that the calcium channel blocker group, one of which is nicardipine, can increase the achievement of goals in mean arterial pressure (MAP) in preventing the progression of organ damage. This study aimed to evaluate the use of nicardipine therapy on the MAP and blood pressure (BP) in patients with hypertension crisis. The research design was cross-sectional with statistical analysis – retrospective data collection at Hajj General Hospital Surabaya for August to December 2021. The number of samples in this study matched the inclusion criteria; 20 patients were obtained, 16 with a diagnosis of hypertension emergency, and four with hypertension urgency who received single or combined intravenous nicardipine therapy  $<0.005$  with an average BP decrease of pre  $20.375 \pm 31.492 / 103.50 \pm 10.400$  mmHg and post  $121.34 \pm 14.364 / 81.80 \pm 11.186$  so that intravenous nicardipine therapy was significant in reducing systolic and diastolic BP. In the profile of the MAP value statistically using the paired T-test, it was found that the P-value was  $0.000 < 0.005$  with a decrease in the MAP pre-value of  $135.028 \pm 13.8857$  mmHg and post  $93.650 \pm 8.9499$  mmHg, showing a reduction in MAP as expected. In conclusion, using nicardipine intravenously at a 5 mg/hour dose has shown an optimal decrease in BP and MAP in hypertensive emergency and urgency patients.

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## INTRODUCTION

Hypertension is still the number one cause of death in the world every year. If the blood pressure (BP) is more than 140/90 mmHg, it is stated as hypertension with or without accompanied by damage/threat of target organ damage; the condition is called crisis hypertension<sup>1</sup>. A hypertensive crisis is an acute increase in systolic blood pressure (SBP) and diastolic blood pressure (DBP) above 180/120 mmHg, or SBP more than 200 mm Hg and/or DBP more than 120 mm Hg<sup>2</sup>. Hypertensive crises can be divided into hypertensive emergencies and urgency<sup>3,4</sup>. Hypertensive urgency is hypertension without target organ damage<sup>5</sup>. A hypertensive emergency is a hypertension with evidence of ongoing or acute target organ damage that requires appropriate pharmacological intervention to lower systemic BP<sup>6</sup>.

In treating hypertensive urgency patients, because there are no indications of severe organ damage, the use of oral drugs to lower BP gradually and controlled for 24 to 48 hours<sup>7</sup>. Meanwhile, a hypertensive emergency is a decrease in SBP by using short-acting antihypertensive drugs, such as antihypertensives given intravenously to prevent the progression of further organ damage or even mortality (death) if this hypertension is not treated quickly and appropriately<sup>8</sup>. The

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recommendations for hypertension emergencies "ESC/ESH Guidelines for the management of arterial hypertension" are esmolol, metoprolol, labetalol, fenoldopam, clevidipine, nicardipine, nitroglycerin, nitroprusside, enalaprilat, and clonidine<sup>9</sup>. Meanwhile, for hypertensive urgency, including the beta blockers labetalol, centrally acting clonidine, the ACE inhibitor captopril, and the alpha-blocker prazosin, calcium channel blockers (CCB) such as amlodipine, felodipine, isradipine, and nifedipine have been given sublingually for a faster onset<sup>10</sup>.

One of the therapies for hypertension crisis is the CCB group, which is divided into the dihydropyridine and the non-dihydropyridine group. Calcium channel blocker effectively lowers BP, alone or in combination<sup>11</sup>. Calcium channel blocker has a mechanism of action by blocking extracellular  $Ca^{++}$  channels from entering the cell, resulting in the relaxation of vascular smooth muscle and decreased cardiac muscle contraction. This causes vasodilation and a corresponding decrease in BP<sup>12</sup>. Nicardipine is a dihydropyridine calcium antagonist that is often used in the treatment of hypertensive emergencies<sup>13</sup>. This is supported by the statement<sup>14</sup> that nicardipine is the first line of treatment in managing hypertensive emergencies. Nicardipine is usually infused at 5-15 mg/hour. This drug has a rapid onset of action of 5-10 minutes with a duration of action of 15-90 minutes with a stable effect and minimal effect on heart rate<sup>15</sup>. According to Malesker and Hilleman<sup>16</sup>, nicardipine with nitroglycerin resulted in a faster decrease in BP in nicardipine patients with a time of 7.7 hours with an average SBP of 94 mmHg while nitroglycerin only fell after 11.9 hours with an average SBP of 108 mmHg. Nicardipine was significantly greater than labetalol in achieving BP targets: nicardipine by 83% and labetalol by 67%.

The results of a preliminary study conducted by researchers at the Emergency Room of the Hajj General Hospital Surabaya, showed that the number of visits by hypertension patients in the Emergency Room was quite large, and the hospital was also a referral hospital. Other data obtained through simple interviews with health workers is the number of hypertensive crisis patients treated in the emergency department. However, research has yet to be conducted regarding antihypertensive therapy's effectiveness in treating hypertensive crisis patients. Based on the above description of the importance of proper use of antihypertensive drugs for hypertensive crisis patients, the therapy given must be carried out appropriately to save the patient's life and can extend the patient's life span and based on observations at a Hajj General Hospital Surabaya, the researcher is interested in conducting research with research objectives to evaluate the use of nicardipine therapy on the mean arterial pressure (MAP) and BP in patients with hypertension crisis.

## MATERIALS AND METHODS

### *Materials*

The type of research was observational, with a cross-sectional study design with statistical analysis to evaluate the use of nicardipine therapy on the MAP and BP in patients with hypertension crises. The data was retrospective in the form of medical records of patients diagnosed with hypertensive urgency or emergency crisis in an inpatient ICU at a Hajj General Hospital Surabaya from August to December 2021. This study used secondary data: the medical records of patients who met the study's inclusion criteria.

### *Methods*

#### *Study design*

This research study was an observational retrospective with a non-probability sampling consecutive sampling technique. The research has been declared ethically feasible through an ethical committee test at the Ethics Committee Institute, Universitas Surabaya, and declared ethically feasible with an ethical permit 35/KE/IV/2022.

#### *Study location*

The study was conducted at the Hajj General Hospital Surabaya, which is located in Klampis Ngasem, Sukolilo, Surabaya, East Java, Indonesia, in the ICU inpatient room.

#### *Sample size calculation*

The number of samples in this study was 20 patients aged 18 years were for in this study. The population in this study were medical records of patients with hypertension crisis at Hajj General Hospital Surabaya from August to December 2021. The sample in this study was medical records of inpatients ICU patients with a diagnosis of hypertension crisis (urgency or

emergency) who were treated with antihypertensive nicardipine intravenously at Hajj General Hospital Surabaya in the period August – December 2021. Sampling was carried out using a non-probability sampling technique using consensual sampling: including all subjects who met the inclusion criteria in the study.

#### *Inclusion criteria*

1. Inpatient ICU patients diagnosed with hypertensive crisis (urgency or emergency) with an age range above >18 years who are treated with intravenous antihypertensive nicardipine at Hajj General Hospital Surabaya from August to December 2021.
2. Hypertensive patients with nicardipine drug therapy alone or in combination with (other antihypertensives) who have data in the form of measurement results of SBP, DBP, and MAP.

#### *Exclusion criteria*

1. Incomplete patient medical record data.
2. Patients receiving analgesic therapy.

#### *Statistical analysis*

Data analysis was performed using the SPSS statistical program. Descriptive statistics were used to determine the patient's characteristics; a normality test was carried out before statistical tests. Data analysis consisted of univariate analysis and bivariate analysis using a T-test dependent paired sample and a T-test independent paired sample, with a significance level of 0.05.

## RESULTS AND DISCUSSION

#### *Patient characteristics*

The number of samples in this study that matched the inclusion criteria was 20 patients during the study period: 16 with a diagnosis of hypertension emergency and four with hypertension urgency who received single or combined intravenous nicardipine therapy. Data on the characteristics of critically hypertensive patients in this study included gender, age, comorbidities, pulse rate, and therapy regimen. The description of patient characteristic data can be seen in **Table I**. The data on the characteristics of the research sample can be seen in **Table I** of the patient characteristics: gender and age of the accompanying patient. From **Table I**, it can be seen that the majority of the male sex experienced crisis hypertension. Males in the general population have the highest DBP rates compared to women of all ages, and males also have the highest prevalence rates for hypertension<sup>17</sup>. The reason for lifestyle is that men tend to do more activities, so fatigue accompanied by an unhealthy diet and lifestyle is one of the factors for hypertension<sup>18</sup>. The characteristics of the age range included in this study were >18 years, where the patient sample in this study was dominated by the age range of 56-65 years in the late elderly category. Individuals over 40 years will experience a condition where the walls of blood vessels will experience a loss of elasticity. Such conditions will result in increased BP on the walls of blood vessels because blood continues to pump without dilatation of blood vessels<sup>19</sup>.

The sample of patients in the study of diagnosing hypertension emergencies was more dominant with stroke complications. A stroke is a sudden loss of brain function caused by an interruption of blood flow to the brain (ischemic stroke) or the rupture of a blood vessel in the brain (hemorrhagic stroke). Impaired blood flow or rupture of a blood vessel causes brain cells (neurons) in the affected area to die<sup>20</sup>. World Health Organization stated that stroke is a clinical sign that develops rapidly due to focal (or global) disturbance of brain function, with symptoms lasting 24 hours or more, which can lead to death in the absence of causes other than vascular<sup>21</sup>.

Clinical manifestations of a hypertensive emergency are hypertension with evidence of ongoing or acute target organ damage (encephalopathy, intracerebral hemorrhage, acute left ventricular failure with pulmonary edema, unstable angina, aortic aneurysm dissection, AML, eclampsia, micro-angiopathic hemolytic anemia or insufficiency renal) that require appropriate pharmacological intervention to lower systemic BP<sup>22</sup>. In general, the pulse rate in this crisis hypertensive patient is normal (70-80 beats per minute) in both hypertensive emergencies by 40% and urgency by 20%. An increase in pulse rate is usually accompanied by a decrease in stroke volume or total peripheral resistance (RPT), which can influence the

development of hypertension. An increase in pulse rate above 100 beats per minute indicates that there is organ damage in hypertensive patients<sup>23</sup>.

The antihypertensive therapy regimen used in this study to treat crisis hypertension was, in general, 14 patients with single intravenous nicardipine, two patients combined intravenous nicardipine + nimodipine orally, three patients combined IV nicardipine + amlodipine orally + candesartan orally and two patients combined IV + nimodipine orally + amlodipine orally + candesartan orally for one patient. One of the therapies for hypertension crisis is the CCB group, which is divided into the dihydropyridine and the non-dihydropyridine group. Calcium channel blocker effectively lowers BP, alone or in combination<sup>24</sup>. Nicardipine is a dihydropyridine calcium antagonist that is often used in the treatment of hypertensive emergencies. This is supported by the statement<sup>25</sup> that nicardipine is the first line of treatment in managing hypertensive emergencies. Nicardipine is usually infused at 5-15 mg/hour. The use of antihypertensives for the treatment of hypertensive crisis is primarily using combination therapy, namely a combination of nicardipine with other antihypertensives. Therapy to overcome crisis hypertension must have a rapid onset of action, be easily titrated, and be safe, considering that BP must be lowered immediately within 24 hours to prevent organ damage<sup>26</sup>.

**Table I.** Patient characteristics

Patient characteristics		Hypertension emergency		Hypertension urgency	
		Total (N)	%	Total (N)	%
<b>Gender</b>	Man	11	55	3	15
	Female	5	25	1	5
<b>Age (years)</b>	Early elderly (46-55)	5	25	2	10
	Late elderly (56-65)	8	40	2	10
	Seniors (>65)	3	15	0	0
<b>Comorbidities</b>	No comorbidity	0	0	4	20
	Stroke	12	60	0	0
	Diabetes Mellitus	2	10	0	0
	Chronic kidney disease	2	10	0	0
<b>Pulse</b>	70-80 time per minute (normal)	14	70	4	20
	>100 time per minute	2	10	0	0
<b>Therapy regimen</b>	Intravenous nicardipine	10	50	4	20
	Intravenous nicardipine + nimodipin orally	3	15	0	0
	Intravenous nicardipine + amlodipine orally + candesartan orally	2	10	0	0
	Intravenous nicardipine + nimodipin orally + amlodipin orally + candesartan orally	1	5	0	0

#### Nicardipine dosage

Data on intravenous nicardipine doses in patients with a diagnosis of hypertensive crisis in this study can be seen in **Table II**. The average dose of nicardipine is for hypertensive emergencies 4.03125 mg and for hypertensive urgency 3.625 mg. The mean dose of nicardipine intravenously in patients diagnosed with the hypertensive crisis in this study was 4.03125 mg in hypertensive emergencies and 3.625 mg in hypertension urgencies. Based on the literature<sup>27</sup>, nicardipine can be given intravenously by infusion of 100 µg/mL for the short-term treatment of hypertension. At the start of treatment for hypertensive crisis, a dose of 5 mg/hour (increase if necessary), up to a maximum of 15 mg/hour, and then reduced to 3 mg/hour or until the desired BP reduction is achieved. The onset of action of IV nicardipine is 5 to 15 minutes, with a duration of action of 4 to 6 hours. So that the average dose of nicardipine in this study is still within the range according to the effective dose.

**Table II.** Average dose of nicardipine intravenously

Antihypertensive drugs	Hypertension emergency	Hypertension urgency
Average dose of nicardipine intravenous (mg)	4.03125	3.625

#### SBP-DBP profile of hypertensive crisis patients pre- and post-administration of nicardipine intravenously

The SBP-DBP profile of hypertensive crisis patients pre- and post-administration of IV nicardipine were shown in **Table III**. Based on the pre- and post-BP profile, IV nicardipine was given in hypertensive emergencies with an average BP of 210/104 mmHg before post-BP of 119/82 mmHg. In hypertension urgency with an average pre-BP of 195/100 mmHg to post-BP of 130/85 mmHg.

**Table III.** SBP-DBP profile of hypertensive crisis patients pre and post administration of nicardipine intravenously

Hypertensive crisis category	Number of patients	Pre-SBP-DBP conditions (mmHg)			Post-SBP-DBP conditions (mmHg)		
		Average	Min-Max SBP	Min-Max DBP	Average	Min-Max SBP	Min-Max DBP
Hypertension emergency	16	210/104	150-280	90-120	119/82	88-140	54-97
Hypertension urgency	4	195/100	190-200	90-110	130/85	120-140	80-90

#### *Changes of SBP-DBP in hypertensive crisis patients pre- and post-administration of nicardipine intravenously*

In the profile of SBP-DBP in crisis hypertensive patients pre- and post-administration of nicardipine intravenously, in hypertensive emergencies with an average BP of pre 210/104 mmHg to post-BP of 119/82 mmHg. In hypertension urgency with an average pre-BP of 195/100 mmHg to post-BP of 130/85 mmHg, and based on statistical analysis using the Paired T-test in **Table IV**, the P-value of 0.000 < 0.05 indicates that intravenous nicardipine therapy is significant in reducing SBP and DBP with an average pre-BP value of 203.75±31.492/103.50±10.400 mmHg and post-BP of 121.30±14.364/81.80±11.186 mmHg. This is in line with the research results<sup>16</sup> concluded that the use of intravenous nicardipine in hypertensive emergency and emergency crises patients demonstrated optimal BP reduction. Achieving optimal BP reduction must be rapid, reversible, and easily titrated without causing side effects. The goal is to prevent the progression of target organ damage<sup>28</sup>. Target organ damage that can occur such as hypertensive encephalopathy, acute aortic dissection, eclampsia, and acute myocardial infarction<sup>29</sup>. It can be concluded that intravenously with therapeutic doses of nicardipine can decrease SBP and DBP in patients with hypertensive emergencies and urgency crises. Based on the results of the study, the impact of public health, especially in health services, is to provide information to medical personnel about the effectiveness of the use of anti-hypertensive drugs so that they can improve the quality of service to the community by diagnosing hypertension, emergency and urgency crises<sup>28</sup>.

**Table IV.** Changes of SBP-DBP in hypertensive crisis patients pre- and post-administration of nicardipine intravenously

Blood pressure	Pre-BP value (mmHg)	Post-BP value (mmHg)	CI 95%	P-value
	Mean±SD	Mean±SD		
SBP	203.75±31.492	121.30±14.364	66.758±98.142	0.000
DBP	103.50±10.400	81.80±11.186	16.348±27.052	0.000

#### *Profile of MAP values in hypertensive crisis patients pre- and post-administration of nicardipine intravenously*

The profile of MAP pre- and post-administration of nicardipine intravenously was shown in **Table V**. The results show hypertensive emergencies with an average pre-MAP of 136 mmHg to post-MAP of 92 mmHg. In hypertension urgency, the average pre-MAP is 129 mmHg, while post-MAP is 99 mmHg.

**Table V.** Profile of MAP values in hypertensive crisis patients pre- and post-administration of nicardipine intravenously

Hypertensive crisis category	Number of patients	Pre-MAP value (mmHg)		Post-MAP value (mmHg)	
		Average	Min-Max	Average	Min-Max
Hypertension emergency	16	136	114.75-162	92	73.2-107.5
Hypertension urgency	4	129	120-137	99	92-102

#### *Changes of MAP values in hypertensive crisis patients pre- and post-administration of nicardipine intravenously*

The profile of MAP values in hypertensive crisis patients pre- and post-administration of nicardipine intravenously, which was seen descriptively, showed that in hypertensive emergencies, the average pre-MAP of 136 mmHg to post-MAP of 92 mmHg—meanwhile, an average pre-MAP of 129 mmHg to post-MAP of 99 mmHg was recorded in the hypertension urgency. Based on statistical analysis using Paired T-test, the P-value is 0.000 < 0.05, indicating that intravenous nicardipine therapy is significant in reducing the MAP with a pre-MAP value of 135.028±13.8857 mmHg and post-MAP of 93.650±8.9499 mmHg, thus showing a decrease in MAP as expected, as shown in **Table VI**. When using parenteral antihypertensives in hypertensive emergency patients, it is desirable to carefully monitor the decrease in MAP every hour, 2-3 hours, and the next 24 hours. The decrease in MAP in the first hour is expected to reach 10%, followed by the next 2-3 hours by 15%, and then after 24 hours reaches 20-25%. These conditions suggest that the decrease in MAP in hypertensive emergency patients should be monitored gradually. The purpose of this gradual monitoring is to prevent the heart and blood vessels in the brain from hypoperfusion<sup>30</sup>. The appropriate CCB group given to hypertensive urgency patients is

nicardipine at a dose of 30 mg, which can be repeated every eight hours. This is because nicardipine has a fast, stable antihypertensive effect and has minimal effect on heart rate<sup>31</sup>. Based on the results of a study, using nicardipine can reduce MAP by no more than 25%<sup>32</sup>. Selection of the right antihypertensive can lead to achieving the desired MAP (reaching less than 25%) and preventing target organ damage<sup>30</sup>.

**Table VI.** Changes of MAP values in hypertensive crisis patients pre- and post-administration of nicardipine intravenously

Number of patients	Value of pre-MAP (mmHg)	Value of post-MAP (mmHg)	CI 95%	P
	Mean±SD	Mean±SD		
20	135.028±13.8857	93.650±8.9499	35.3328±474222	0.000

## CONCLUSION

Based on the study, it was concluded that the use of nicardipine with the average dose for hypertensive emergencies was 4.03125 mg, and hypertension urgency was 3.625 mg. The results indicate that IV nicardipine can significantly change the decrease in SBP and DBP with BP values the average pre-administration of 203.75±31.492/103.50±10.400 mmHg and post-administration of 121.30±14.364/81.80±11.186 mmHg, and can reduce the pre-MAP of 135.028±13.8857 mmHg and post-MAP of 93.650±8.9499 mmHg.

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## AUTHORS' CONTRIBUTION

**Selly Septi Fandinata:** conceptualization, methodology, formal analysis, writing – original draft, writing – review & editing, fundraising. **Rizky Darmawan:** formal analysis, methodology. **Ninik Mas Ulfa:** investigation, writing – original draft. **Deddy Aryanda Putra:** review & editing, supervision.

## DATA AVAILABILITY

None.

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

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