

Comparison effectiveness of use antihypertensive in preeclampsia patient in RSUD Panembahan Senopati Bantul

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ABSTRACT

Preeclampsia is one of many unsolved obstetric problems. The purpose of this research is to compare effectiveness of antihypertensive in preeclampsia patient in RSUD Panembahan Senopati Bantul in the period January-July 2019. This study needs to analyze about antihypertensive drugs in preeclampsia because Preeclampsia is the 3rd rank of disease in pregnancy that causes maternal death after hemorrhagic and cardiovascular diseases. The study was conducted at Panembahan Senopati Hospital Bantul because hypertension in inpatient was ranked first in 10 distributions of non-communicable diseases. The research was observational analytic using a cross sectional study with retrospective data collection of patient medical record. Samples were selected on inclusion and exclusion criteria in 46 cases. Data analysis using Mann-Whitney to determine differences in drug effectiveness and Fisher's to determine the relationship. The results are found that no relationship between maternal age, obstetrical age, pregnancy status, method of birth, and length of stay, but there was a relationship between the severity of preeclampsia with the achievement of blood pressure targets. The results of comparative analysis of the effectiveness nifedipine monotherapy with combination of nifedipine + methyldopa there was a significant difference ($p = 0.006$), and there was a significant relationship between nifedipine monotherapy and combination of nifedipine + methyldopa ($p = 0.015$) OR results = 7.200. The conclusion of this study is more effective to use the combination of nifedipine + methyldopa for patients with preeclampsia.

Keywords: preeclampsia, drug effectiveness, antihypertension, nifedipine monotherapy, combination of nifedipine and methyldopa

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INTRODUCTION

Preeclampsia is a disease characterized by hypertension, edema, and proteinuria that occurs during pregnancy (Prawirohardjo, 2018). Preeclampsia is the 3rd rank of disease in pregnancy that causes maternal death after hemorrhagic and cardiovascular diseases (Cunningham, et al., 2014). The study was conducted at Panembahan Senopati Hospital Bantul because hypertension in inpatient was ranked first in 10 distributions of non-communicable diseases (Dinkes Bantul, 2019). The choice of antihypertensive treatment can prevent other complications and protect the mother and fetus from the risks. The first line of antihypertensive treatment in preeclampsia is labetalol, while the second line is methyldopa and nifedipine (JNC 8, 2014). In this study, treatment with monotherapy nifedipine and a combination of nifedipine + methyldopa was used. Based on Indhayani's research (2018), monotherapy nifedipine treatment can reduce blood pressure by 7.14 ± 5.23 mmHg (Indhayani, 2018).

Target blood pressure achievement for mild preeclampsia $<140/90$ mmHg and severe preeclampsia $<150/90$ mmHg (Queensland Clinical Guidelines, 2015). Because of that, the study aims to determine the effectiveness of antihypertensive drugs based on the achievement of blood pressure targets and length of stay in Panembahan Senopati Hospital Bantul.

MATERIALS AND METHOD

Study design

This research is an analytic observational study using a cross sectional study using retrospective data collection with patient medical record data. The sampling technique used purposive sampling method in the period January-July 2019. The target blood pressure is achieved according to the Queensland standard of therapy, achieved if BP $<140/90$ mmHg for mild preeclampsia and BP $<150/90$ mmHg for severe preeclampsia.

Sample

The sample in this study were all inpatients with a diagnosis of hypertension with a pregnant condition who were treated at the Panembahan Senopati Hospital Bantul in the period January-July 2019 and met the inclusion criteria.

Inclusion Criteria:

Adult patient (>18 Years)

Hospitalized pregnant patients with a diagnosis of preeclampsia (BP $> 140/90$ mmHg).

Patients with proteinuria with lab data showing at least +1.

Preeclampsia patients receiving antihypertensive drugs.

Patients with medical record code medical record code O14.0, O14.1, and O14.

Exclusion Criteria:

Patients with illegible and incomplete medical records, no data on blood pressure, proteinuria, or edema, a diagnosis of preeclampsia/ severity of preeclampsia, drugs given (drug name, dose, duration of use), and length of stay.

Tools and Materials

The tools used are pencils, notebooks, laptop, SPSS Version 27. The material used in this study was demographic data tables, medical record data of preeclampsia patients who met the inclusion criteria (patient blood pressure data, use of antihypertensives).

Data Analysis

In this study, relationship analysis and comparison were carried out using SPSS version 27. The relationship analysis was analyzed using Fisher's exact test and comparative analysis using the Mann-Whitney test.

In analyzing the relationship using Chi-Square test. Where the Chi-Square test has requirements in the form of no cells with an observed value of zero, cells with an expected value of less than five, and a maximum of 20% of the number of cells (Dahlan, 2014). So if the results of the relationship analysis do not meet the requirements of the Chi-Square test, an alternative is used in the form of Fisher's Test.

Comparative analysis using Shapiro-Wilk because the sample was <50 and tested for homogeneity using Levene Statistics. If the data is normally distributed ($p > 0.05$) then an analysis is performed using an unpaired t-test. If the data is not normally distributed ($p < 0.05$) then the Mann-Whitney test is used.

If the result using SPSS Version 27 was P Value > 0.05 there was no relationship, or there was no significant data.

RESULT AND DISCUSSION

This study is a non-experimental study with a retrospective method that aims to determine the effectiveness of antihypertensive drugs for the treatment of preeclampsia with ICD codes O14.0, O14.1, and O14.9 in Panembahan Senopati Hospital Bantul by looking at the achievement of blood pressure targets in respondents. This research was conducted with permission from the ethics commission of Aisyiyah University Yogyakarta no. protocol 3404012S121242019120300007. The data used to see effectiveness of antihypertensive using the medical record data of preeclampsia patients hospitalized during January-July 2019. The sample of this study is 46 cases of patients.

Table 1 shows that there isn't a relationship between the mother's age and the achievement of blood pressure targets. Mother's age less than 20 years old, reproductive organs are not perfect, and Mother's age more than 35 years old, the organs have started to weaken. The higher mother's age, the higher risk for preeclampsia (Prawirohardjo, 2018). The different result from Haskel, et al (2018), older mothers increased the rate of postpartum presentation, $p = 0.01$ (Haskel, et al., 2018). Based on result research Asmana, et al (2016) at the Achmad Mochtar Bukit Tinggi Hospital in the period 2012-2013, there was a relationship between mother's age and severe preeclampsia with ages <20 years old and >35 years old as risk factors for the occurrence of preeclampsia. (Asmana et al., 2016). The relationship between maternal age based on Table 1 also shows that there isn't relationship between gestational age and blood pressure target achievement. The same result was with Miasih (2016) at Wates Hospital at >37 weeks of gestation (83.33%) (Miasih, 2016). The results of gravida status in Table 2 also show no relationship between gravida status and the achievement of blood pressure targets. The results are different from another research, which found that 60% had preeclampsia with primigravida status (Grum et al., 2017). The results indicate that there is no relationship between parity and the achievement of blood pressure targets. The results of the study are in accordance with other research that preeclampsia was diagnosed as having primipara (53.3%), but the data analysis has no relationship (Muthoharoh et al., 2016).

Based on the results of the study, according to Table 1, there is no relationship between a history of abortion and the achievement of blood pressure targets. Same result with Bangkele, et al (2016), There is no relationship between abortion and the incidence of preeclampsia in pregnant women, $p = 0.345$ (Bangkele et al., 2016). This study inform that there was no relationship between the method of birth and the achievement of blood pressure targets. Its difference from other research is that there is a relationship between blood pressure and the method of birth. If a woman has a high BP, then the risk factor for a cesarean section (Van der Tuuk et al., 2017).

Meanwhile, the results of the analysis are in accordance with Table 1 for the diagnosis of preeclampsia. There was two Diagnosis of preeclampsia which is Patients with blood pressure measurements $>140/90$ mmHg, proteinuria data that is $>+1$ for mild preeclampsia, and blood pressure measurements $>160/110$ mmHg, proteinuria data that is $>+3$. The classification on achieving blood pressure targets is not valid because the data are not comparable, and there is bias because Panembahan Senopati Bantul Hospital was a referral hospital, so patients will come to the hospital with condition severe preeclampsia. Other research at the Sleman Hospital results in more patients with a diagnosis of severe preeclampsia (34 respondents) (Julianti, 2017). Based on the length of stay,

patients with preeclampsia were treated for < 5 days, and as shown in [Table 2](#), the results showed that there was no relationship between length of stay and achieving blood pressure targets. In accordance with research conducted by Guerrier, et al, the results of the length of hospitalization for preeclampsia and eclampsia cases were 4 days ([Guerrier, et al., 2013](#)).

Mechanism of action Nifedipine (category C) is a class of calcium channel blockers that has a strong vasodilating effect. While methyldopa (Category B) is a class of adrenergic blockers that reduce sympathetic nerve activity. The use of the combination of nifedipine + methyldopa can reduce blood pressure maximally and prevent other complications ([ESC, 2018](#)). This study used Nifedipine And Methyldopa Because The first line Antihypertensive in Preeclampsia is Labetalol, and the second line is Methyldopa And Nifedipine ([JNC 8, 2014](#)). and There is A Previous Research, Indhayani's (2018) using Single Nifedipine Treatment Can Reduce Blood Pressure By 7.14 ± 5.23 mmhg ([Indhayani, 2018](#)). Base on national Formularium, Panembahan Senopati Hospital Bantul doctors use Nifedipin + Metildopa and Nifedipin for preeclampsia patients.

Table 1. Analysis of the relationship between the characteristics of preeclampsia inpatients and the achievement of blood pressure targets at Panembahan Senopati Hospital Bantul for the January-July 2019 Period (N=46)

Characteristics of Respondent		Achievement of Blood Pressure Targets		Total (n(%))	P Value	OR (CI 95%)
		Not Achieved (n(%))	Achieved (n(%))			
Mother's Age	<20 and >35 Years Old	7 (25%)	21 (75%)	28 (60.9%)	0.548	0.867 (0.227-3.210)
	21 -34 Years Old	5 (27.8%)	13 (72.2%)	18 (39.1%)		
Gestational Age	≤37 Weeks	4 (26.7%)	11,1 (73.3%)	15 (32.6%)	0.608	1.045 (0.248-4.235)
	>37 Weeks	8 (25.8%)	23 (74.2%)	31 (67.4%)		
Gravida Status	Primigravida	4 (36.4%)	7 (63.6%)	11 (23.9%)	0.302	1.929 (0.448-8.304)
	Multigravida	8 (22.9%)	27 (77.1%)	35 (76.1%)		
Parity	Never	9 (27.27%)	24 (72.73%)	33 (71.7%)	0.457	1.389 (0.335-5.755)
	>1	3 (23.1%)	10 (76.9%)	13 (28.3%)		
Abortion History	Never	11 (29.7%)	26 (70.3%)	37 (80.4%)	0.245	3.385 (0.377-30.398)
	>1	1 (11.1%)	8 (88.9%)	9 (19.6%)		
How To Give Birth	Caesar	0 (0%)	10 (100%)	10 (24.4%)	0.058	1.409 (1.125-1.765)
	Normal	9 (29%)	22 (71%)	31 (75.6%)		
Long of Stay	≤5 Days	9 (25.7%)	26 (74.3%)	35 (76.1%)	0.601	0.923 (0.200-4.255)
	>5 Days	3 (27.3%)	8 (72.7%)	11 (23.9%)		

As [Table 2](#) shows the results of data analysis there is a significant difference between nifedipine monotherapy and the combination of nifedipine + methyldopa. The results of the analysis of the relationship as shown in [Table 3](#) show the results of the relationship between monotherapy and combination on achieving blood pressure and nifedipine monotherapy 7.200 times the chance of not achieving the blood pressure target compared to the combination drug nifedipine + methyldopa. So based on the results of the study, it was more effective to treat using a combination of nifedipine + methyldopa for preeclampsia. The same result with [Pratiwi, et al \(2013\)](#) is combination of nifedipine and methyldopa is effective in lowering blood pressure, $p = 0.0001$ ([Pratiwi, et al., 2013](#)). Another

study found that nifedipine monotherapy is able to lower blood pressure more effectively than the combination of nifedipine and methyldopa (Velusamy, 2017). Another similar study found that the use of nifedipine monotherapy in preeclampsia patients was 22.1% and the combined use of nifedipine + methyldopa was 44.6%, the combination of nifedipine + methyldopa was obtained from systolic blood pressure of 165 +/- 25 mm Hg to a decrease of 150 +/- 10 mmHg (p = 0.021) and at diastolic blood pressure of 102 +/- 12 mmHg to 93 +/- 07 mmHg (p = 0.022) (Nandini, et al., 2016).

Regarding the long-term safety of using nifedipine and methyldopa, the use of nifedipine in doses greater than >60 mg may increase the risk of adverse events such as tachycardia and hypotension. Meanwhile, methyldopa can cause sedation, drowsiness, dry mouth, depression, postural hypertension, rebound hypertension, withdrawal syndrome, and some autoimmune events (Alatas, 2019). However, in this study, it cannot be concluded whether the respondent experienced side effects from the drug or not because the patient's medical record does not include any reports of side effects from the use of the two drugs, but it is still necessary to know the unwanted effects of the use of the two drugs in order to monitor and maintain the health of mothers and children.

Table 2. Analysis of the relationship between diagnosis of preeclampsia and achievement of blood pressure targets at Panembahan Senopati Hospital, Bantul period January-July 2019

Diagnosis	Medicine	Achievement of Blood Pressure Targets		Total(n(%))	P Value	OR (CI 95%)
		Not Achieved (n(%))	Achieved (n(%))			
Mild Preeclampsia	Nifedipin	9 (47.4%)	10 (52.6%)	19 (41.3%)	0.000	OR value does not appear
	Combination of Nifedipin + Metildopa	0 (0%)	0 (0%)	0 (0%)		
Severe Preeclampsia	Nifedipin	0 (0%)	0 (0%)	0 (0%)	0.000	
	Combination of Nifedipin + Metildopa	3 (11.1%)	24 (88.9%)	27 (58.7%)		

Table 3. Comparative analysis and analysis of the relationship between respondents' blood pressure target achievement in preeclampsia at Panembahan Senopati hospital Bantul for the January-July 2019 period

Medicine	Achievement of Blood Pressure Targets		Total	P Value (Mann-Whitney)	P Value (Fisher)	OR (CI 95%)
	Not Achieved (n(%))	Achieved (n(%))				
Nifedipin	9 (47.4%)	10 (52.6%)	19 (41.3%)	0.006	0.015	7.200 (1.606-32.285)
Combination of Nifedipin + Metildopa	3 (11.1%)	24 (88.9%)	27 (68.7%)			
Total	12 (26.1%)	34 (73.9%)	46 (100%)			

The results in Table 4 show that there is no significant relationship between drug administration and length of stay. Nifedipine monotherapy drug with length of stay <5 days (Ainuddin, et al., 2019). The result of this research is that have been carried out are in accordance with previous studies where

the administration of the monotherapy nifedipine on length of stay <5 days but there is no relationship between drug administration and length of stay.

The limitation of the study is there is still a lack of sample needed because the limited sample makes the analyzed data unbalanced or disproportionate between one and another. Suggestions for further researchers are expected to carry out further research related to the analysis of the effectiveness of antihypertensive therapy in preeclampsia patients with a larger sample and pay attention to the patient's lifestyle and can also analyze the safety level of antihypertensive therapy after use in preeclampsia patients. For hospitals, it is necessary to record patient medical records which are inputted on a computer so that it can simplify and minimize errors in data collection so that the data obtained is more valid.

Table 4. The relationship of drug administration to length of hospitalization for preeclampsia patients at Panembahan Senopati hospital Bantul for the January-July 2019 period

Medicine	Long of Stay		P Value	OR (CI 95%)
	≤5 Days (n(%))	>5 Days (n(%))		
Nifedipin	16 (84.2%)	3 (4.5%)	0.234	2.246 (0.509-9.907)
Combination of Nifedipin + Metildopa	19 (20.5%)	8 (6.5%)		

CONCLUSION

The results of the comparative analysis of effectiveness were that there was a significant difference between nifedipine monotherapy and a combination of nifedipine + methyldopa and the use of a combination of nifedipine + methyldopa was more effective than nifedipine monotherapy and there was a significant relationship between the administration of nifedipine monotherapy and the combination of nifedipine + methyldopa on blood pressure achievement with p value = 0.015 and the value of OR = 7.200.

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