Research Article

Evaluation of Therapy in Preeclampsia Patients in Several Public and Private Hospitals

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Abstract

Objective: To determine the rationality and effectiveness of therapy in preeclampsia patients at the Inpatient Installation of several public and private hospital in Banyumas area from January-December 2021.

Methods: This study is retrospective, employing purposive sampling for data collection. The data were extracted from the medical records of patients diagnosed with pre-eclampsia at the Inpatient Installation. The sample consisted of 212 patients with a confirmed diagnosis of pre-eclampsia.

Results: From this study, it was found that antihypertensive medications given were methyldopa (52.8%), nifedipine (45.2%), and amlodipine (2%). It was found that the results of the five appropriate analyses were the suitable indication, right patient, proper medication, right dose, and correct route (100%). The antihypertensive medications used were effective in reducing the blood pressure of preeclampsia patients (100%), with an average decrease in systolic pressure by 37 mmHg, an average decrease in diastolic pressure by 22 mmHg, and an average decrease in MAP by 28 mmHg.

Conclusion: Antihypertensives given to preeclampsia patients in several public and private hospitals in Banyumas were rational and effective in reducing the patient's blood pressure.

Keywords: antihypertensives, effectiveness, preeclampsia, rationality.

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INTRODUCTION

Pregnant women with preeclampsia have a very high risk of developing eclampsia, HELLP syndrome (Hemolysis, Elevated Liver enzymes, Low Platelets), and an increased risk of death for pregnant women. Moreover, preeclampsia had long-term effects post-delivery, such as increase in blood pressure, BMI, and CRP level [1].In Indonesia, maternal deaths in 2020 were caused by three leading causes, including bleeding as many as 1,330 cases, hypertension/ high blood pressure in pregnancy as many as 1,110 cases, and circulatory system disorders as many as 230 cases[2]. Meanwhile, in 2018, the most common causes of maternal deaths in Central Java included pre-eclampsia/eclampsia (36.80%), hemorrhage (22.60%), infection (5.20%), and other causes (35.40%)[3]. In Banyumas Regency, the prevalence of maternal mortality rate (MMR) is relatively high at 67.84 per 100,000 live births[4].

One of the factors influencing the occurrence of maternal mortality due to pre-eclampsia is the presence of irrational therapy because irrational antihypertensive therapy can cause the risk of hypotension and potential side effects on the fetus, so when choosing medications during pregnancy, the level of maternal and fetal benefits must outweigh the risks to allow safe and rational treatment[5]. According to research, 77 cases

of medication-related problems were found, including wrong indication medications in 8 cases (10.4%), underdose in 53 cases (68.8%), and overdose in 16 cases (20.8%). Medication-related problems can lead to the non-achievement of therapeutic targets in treating pre-eclampsia patients. They can increase the risk that is higher than the benefits obtained[6].

One of the therapies given to pre-eclampsia patients is methyldopa. Methyldopa is an alpha-2 adrenergic receptor agonist antihypertensive medication. It is the first line of hypertension treatment for pregnant women with chronic hypertension because it is the safest and has a large margin of safety. However, methyldopa has minor peripheral effects that can reduce sympathetic tone and arterial blood pressure but do not affect pulse frequency and renal blood flow[7]. Using methyldopa in patients with severe pre-eclampsia can reduce VEGF (Vascular Endothelial Growth Factor) levels by 10% at 250 mg and reduce levels by 57% at 500 mg. Methyldopa can also reduce Mean Arterial Pressure (MAP) to normal limits. The standard value of MAP ranges from 70 to 100 mmHg[8]. This study aimed to determine the pattern of medication use, rationality, and effectiveness of therapy in pre-eclampsia patients at Wijayakusuma Purwokerto Hospital, Banyumas Regional General Hospital, Prof. Dr. Margono Soekarjo Purwokerto Regional General Hospital and Budhi Asih Purwokerto Mother and Child Hospital for January-December 2021.

METHODS

The Muhammadiyah University of Purwokerto Health Research Ethics Commission has ethically approved this research with the numbers KEKP/ UMP/24/1/2022 and KEKP/UMP/19/1/2022. This research is a type of non-experimental research. The research method us in this study is a retrospective method with data collection using purposive sampling. The retrospective method was used because this study requires existing data that occurred in 2021, namely in the form of medical records of pre-eclampsia patients at the Inpatient Installation of Purwokerto Hospital, Banyumas Regional General Hospital, Prof. Dr. Margono Soekarjo Purwokerto Regional General Hospital and Budhi Asih Purwokerto Mother and Child Hospital from January to December 2021.

The research instruments used in this study include data collection sheets, 2016 Indonesia Society of Obstetricians and Gynecologist guidelines, and patient medical records (medical reports). The collected data included patient names, medical record numbers, ages, medication history, disease history, pregnancy history, allergy history, diagnosis, complaints, gestational age, laboratory data, and clinical information (respiration rate, blood pressure, pulse, body temperature). Additionally, the medication list comprised details such as dose, duration, and frequency.

The obtained data were classified based on patient characteristics, including age, disease diagnosis (classified according to pre-eclampsia), gestational age, and medical history. This classification was presented in tabular form. Additionally, the pattern of antihypertensive medication use is depicted as a percentage (%).

The rationality of treatment was assessed by comparing the collected data with the treatment criteria outlined in the official literature, specifically the 2016 Indonesia Society of Obstetricians and Gynecologists guidelines. The results were processed in percentage form and presented in tables. Effectiveness was evaluated through bivariate analysis using the Wilcoxon method, which assesses the relationship or influence between two or more variables.

RESULTS

This study evaluates the rationality and effectiveness of therapy in pre-eclampsia patients at the inpatient installation of Wijayakusuma Purwokerto Hospital, Banyumas Regional General Hospital, Prof. Dr. Margono Soekarjo Purwokerto Regional General Hospital and Budhi Asih Purwokerto Mother and Child Hospital from the period January-December 2021 based on a decrease in blood pressure of pregnant women diagnosed with pre-eclampsia to determine the effectiveness of therapy and five right, namely the right patient, the suitable indication, the right medication, the correct dose and the proper administration to determine the rationality of therapy. Based on the data obtained, there were 928 medical records of pregnant women with mild and severe pre-eclampsia. The number of medical records that met the study's inclusion criteria was 212, and 716 data met the exclusion criteria due to incomplete medical record data, not getting antihypertensive therapy, having no proteinuria lab data, and having a history of hypertension.

Patient Characteristics

The results of the analysis of the characteristics of preeclampsia patients in the inpatient installation of public and private hospitals in Banyumas can be seen in Table 1.

Table 1. Characteristics of Patients Diagnosed with Preeclampsia inpatients Installations of Public and Private Hospitals in Banyumas from January-December 2021

Characteristics	Number of Patients (n = 212)	(%)
Age (Years)		
17-25	49	23.13
26-35	88	41.50
36-45	75	35.37
Gestational Age (weeks)		
0-14	0	0
14-28	6	2.84
28-42	206	97.16
Proteinuria (Dipstick examination)		
+1	76	35.84
+2	52	24.52
+3	75	35.37
+4	9	4.27
Comorbidities		
None	203	95.77
Asthma	5	2.35
Hemorrhoids	1	0.47
Anemia	2	0.94
Scoliosis	1	
Gestational Status		
G1	61	28.77
G2	61	28.77
G3	45	21.22
G4	33	15.59
G5	10	4.71
G6	2	0.94

Pattern of Antihypertensive Medication Use

The analysis of antihypertensive medication use patterns in pre-eclampsia patients in inpatient installations of public and private hospitals in Banyumas can be seen in Table 2.

Table 2. Data on the Use of Antihypertensives in Pre-Eclampsia Patients at Public and Private Hospitals in Banyumas

Medication	Dosage (mg)	Number of Patients	Average Duration of Therapy (Days)
Methyldopa	250	43	2
	500	145	3
Nifedipine	10	165	3
Amlodipine	5	2	1
	10	10	2

Rationality Evaluation of Antihypertensive Treatment

The analysis of the rationality of antihypertensive treatment in pre-eclampsia patients in inpatient installations of public and private hospitals in Banyumas can be seen in Table 3.

Table 3. Rationality of Antihypertensive use in Pre-Eclampsia Patients in Public and Private Hospitals in Banyumas

Rationality Criteria	Amount of Use		(%)	
	Appropriate	Inappropriate	Appropriate	Inappropriate
Right patient	212	0	100	0
Right indication	212	0	100	0
Right medicine	212	0	100	0
Correct dose	212	0	100	0
Correct method of administration	212	0	100	0

Evaluation of the Effectiveness of Antihypertensive Treatment

The results of the analysis of the effectiveness of antihypertensive treatment in pre-eclampsia patients in inpatient installations of public and private hospitals in Banyumas can be seen in Table 4.

Table 4. Effectiveness of Antihypertensive use in Preeclampsia Patients in Public and Private Hospitals in Banyumas

Blood Pressure Value	Before (mmHg)	After (mmHg)
Systolic	160	123
Diastolic	101	79
Mean Arterial Pressure (MAP)	121	93

DISCUSSION

Based on Table 1, the highest age group is the early adult age category (26-35), with as many as 88 patients (41.50%), and late adulthood (36-45), with as many as 75 patients (35.37%). This result parallels previous research on the proportion of pregnant women who experience preeclampsia, with the highest percentage occurring in the age group 20-35 years by 70.59%[9]. Furthermore, another study states that patients diagnosed with preeclampsia with the highest percentage are in the age category 26-35 years and 36-45 years by 43% and 34%[10]. At the age of >30/35 years, it is prone to hypertension and eclampsia, which is caused by changes in tissues and there are also changes in the birth canal that are not as flexible as pregnant women under 30/35 years of age[11,12].

Characteristics of patients based on gestational age, the highest percentage was obtained in the third trimester of pregnancy, namely 206 patients (97.16%). This result parallels previous studies, which found that 100% of the incidence of preeclampsia occurred in third-trimester pregnancy[9,10]. Another study showed that term pregnancy had a higher risk of severe preeclampsia-eclampsia compared with preterm pregnancy. However, the severity of complications in preeclampsia had an association with preterm delivery [13,14]. This result is reciprocal with the theory of placental implant ischemia, which states that preeclampsia increases with increasing gestational age. As fibrinogen levels increase, risk for early-onset preeclampsia are higher in pregnant women. Increased fibrinogen levels are part of an exaggerated inflammatory response and subsequent endothelial activation, which is currently believed to be the primary pathophysiological mechanism in preeclampsia[15].

Preeclampsia patients who have proteinuria levels with the highest percentage are +1, which is 76 patients (35.84%), and +3, as many as 75 patients (35.37%). In preeclampsia, one of the manifestations is proteinuria; usually, much protein passes through the glomerular capillaries but does not enter the urine. Compensation and selectivity of the glomerular all inhibit the transport of albumin, globulin, and other high molecular weight proteins across the glomerular wall. Proteinuria that occurs in preeclampsia results from hypertension in pregnancy that causes blood perfusion in the kidneys and a decrease in glomerular filtration rate so that high molecular weight proteins leave the glomerulus and cause protein in the urine or proteinuria[16].

The most preeclampsia patients were in the G1 / first pregnancy and G2 / second pregnancy categories, namely 61 patients (28.77%). The results of this study are in accordance with the statement that patients who are first pregnant as primigravida are 6-8 times more likely to experience preeclampsia than patients who have been pregnant or multigravida[17]. Furthermore, preeclampsia is more common in patients who first conceive or primigravida compared to patients who have had previous pregnancies or multigravida; this is due to the formation of blocking antibodies caused by stress factors experienced by patients who first conceive or primigravida in the face of childbirth. Gravida status is one of the factors that can influence the incidence of preeclampsia in pregnant women[18].

The use of methyldopa is more often used as therapy if the patient's clinical condition has blood pressure between 140-160/90-110 mmHg; the results of this study are in step with the 2016 Indonesia Society of Obstetricians and Gynecologist reference standard, which states that methyldopa is indicated to lower blood pressure in preeclampsia patients with blood pressure more than 140/90 mmHg. Methyldopa treatment has been reported to prevent the subsequent development of severe hypertension during pregnancy. It has not been shown to affect uteroplacental or fetal hemodynamics or well-being, and associated with fewer adverse infant outcomes, including respiratory distress, seizure and sepsis[19]. While the administration of nifedipine is more often used as therapy if the patient's clinical condition has a blood pressure of more than 160/110 mmHg, the results of this study are consistent with the 2016 Indonesia Society of Obstetricians and Gynecologist reference standard, which states that nifedipine is used if the patient's blood pressure is more than 160/110 mmHg. However, the concomitant use of calcium channel blockers with magnesium sulfate to prevent seizures requires special attention, as the concomitant administration of these medications has been reported to cause circulatory collapse and neuromuscular blockade[19].

Appropriate Patient

Assessment of appropriate patients in this study is based on contraindications to antihypertensives used and compared with the patient's medical

history and whether antihypertensives used in pregnant women are safe or not based on the Pregnancy Risk Category of the medication. Based on research conducted on 212 medical record data for preeclampsia patients at the Inpatient Installation of Public and Private Hospitals in Banyumas for the period January-December 2021. It was found that the value of the accuracy of selecting antihypertensive medications based on the right patient was 100% appropriate for the patient; the assessment of the right patient was based on the patient's pathology and physiological conditions and did not cause contraindications in the patient. Methyldopa is under Pregnancy Risk Category B, acts in the central nervous system, and is the most commonly used antihypertensive medication for pregnant women with chronic hypertension. Methyldopa has a wide safety margin (safest). Contraindications to using methyldopa are for patients with active liver disease (acute hepatitis, cirrhosis hepatitis)[7]. Nifedipine and amlodipine are popular and widely used Pregnancy Risk Category C medications in pregnant women diagnosed with preeclampsia that act as selective, natriuretic renal arteriolar vasodilators and increase urine production. Amlodipine has been used in pregnancy, but safety data are lacking[19]. Excessive use of CCBs has been reported to cause fetal hypoxia and acidosis. This circumstance is due to relative hypotension following CCB administration[7].

Appropriate Indication

Assessment of appropriate indication in this study is based on whether or not antihypertensive treatment is suitable for the diagnosis and blood pressure of the patient. Based on 2016 Indonesia Society of Obstetricians and Gynecologist, antihypertensives are given if the systolic blood pressure is more than 140 mmHg or the diastolic level is more than 90 mmHg. Based on research conducted on 212 medical record data for preeclampsia patients at the Inpatient Installation of Public and Private Hospitals in Banyumas for the period January-December 2021. It was found that the value of the accuracy of selecting antihypertensive medications based on appropriate indications was 100% correct indications; the assessment of appropriate indications was based on the selection of medications for patients, whether according to the doctor's indications and diagnoses. Antihypertensive therapy has not been shown to reduce fetal growth restriction, placental abruption, or superimposed preeclampsia or to improve perinatal outcomes. The most important indication for antihypertensive administration in pregnancy is maternal safety in preventing cerebrovascular disease. However, the decrease in blood pressure should be gradual, not exceeding 25% in 1 hour, to prevent a decrease in uteroplacental blood flow[7]. The goal of treating hypertension in pregnancy is also to protect pregnant women from high blood pressure, which is dangerous and impacts the continuation of pregnancy, growth, and maturation of the fetus[20].

Appropriate Medication

Assessment of appropriate medications in this study is based on the accuracy of the selection of antihypertensive medications that are safe for pregnant women and compared with the 2016 Indonesia Society of Obstetricians and Gynecologist reference standards. Based on research conducted on 212 medical record data for preeclampsia patients at the Inpatient Installation of Public and Private Hospitals in Banyumas for the period January-December 2021. The value of the accuracy of selecting antihypertensive medications based on appropriate medications is 100% appropriate medications according to the reference standards used. Based on 2016 Indonesia Society of Obstetricians and Gynecologist, the antihypertensive medications given are the Calcium Channel Blocker (CCB) group in the form of nifedipine and the α2-adrenergic agonist group in the form of methyldopa and if the patient's blood pressure is 140-160/90-110 mmHg, the patient is given methyldopa. If the patient's blood pressure exceeds 160/110 mmHg, the patient is given nifedipine[7].

Correct Dose

This study's assessment of the correct dose is based on administering antihypertensive medications to patients within the recommended minimum dose and daily dose range based on the 2016 Indonesia Society of Obstetricians and Gynecologist reference standard. Based on research conducted on 212 medical record data for preeclampsia patients at the Inpatient Installation of Public and Private Hospitals in Banyumas for the period January-December 2021. The value

of the accuracy of selecting antihypertensive medications based on the correct dosage was 100% correct dosage according to the reference standards used. According to the 2016 Indonesia Society of Obstetricians and Gynecologist reference standard, nifedipine's recommended peroral dose range is 10-30 mg, amlodipine is 5-10 mg, and methyldopa is 250 mg-500 mg. If the dose is too low, it causes the medication in the blood to have levels below the therapeutic range, which causes the medication to be unable to provide the desired effect. At the same time, if the dose is too high, it causes the medication in the blood to have levels exceeding the therapeutic range, which causes the medication to have a toxic effect[21]. Therefore, administering antihypertensive medications must pay attention to the accuracy of the dose given to patients to obtain therapeutic success and achieve normal blood pressure[22]. Providing medication doses that are not following standards can significantly impact patients. If the dose of medications listed on the prescription is inappropriate, then the patient fails to get the correct treatment related to the disease[23].

The Correct Method of Administration

Assessment of the correct dose in this study is based on when the medication is used as it should be; if the medication has been given according to the instructed method, it can be said to be the right way of administration[24]. Based on research conducted on 212 medical record data for preeclampsia patients at the Inpatient Installation of Public and Private Hospitals in Banyumas for the period January-December 2021. It was found that the value of the accuracy of selecting antihypertensive medications based on the correct method of administration was 100% correct method of administration. Administration of nifedipine is better given orally because using sublingual nifedipine can increase the risk of sudden maternal hypotension and fetal problems due to placental hypoperfusion. Sudden hypotension may be exacerbated by concomitant magnesium sulfate (used as a treatment or prophylactic agent for eclampsia attacks with severe preeclampsia)[20].

Based on Table 4, 212 data showed a decrease in blood pressure after administration of antihypertensive medications. Data from patients with an average initial systolic blood pressure of 160 mmHg and after antihypertensive administration showed a decrease in systolic blood pressure to an average of 123 mmHg, besides that diastolic pressure also decreased from an average initial diastolic blood pressure of 101 mmHg decreased diastolic blood pressure to an average of 79 mmHg and MAP blood pressure also decreased from an average initial MAP blood pressure of 121 decreased MAP blood pressure to an average of 93 (Table 4). This result shows that taking antihypertensive medications reduces blood pressure and is safe for pregnant women without causing side effects for both mother and fetus. These results are parallel with research, which states that in the use of hypertension medications in pre-eclampsia patients, 197 respondents (100%) experienced a decrease in blood pressure after being given antihypertensive medications[25].

Treatment using methyldopa is more often used when the patient's blood pressure is between 140-160/90-110 mmHg; the data is also compatible with the 2016 Indonesia Society of Obstetricians and Gynecologist reference standard, which states that methyldopa is indicated for lowering blood pressure in pre-eclampsia patients, with blood pressure greater than 140/90 mmHg and methyldopa is proven to prevent an increase in the severity of pre-eclampsia disease to severe pre-eclampsia and has no adverse effect on uteroplacental or fetal hemodynamics or fetal well-being[26]. Methyldopa is usually started at 250-500 mg orally 2-3 times daily, with a maximum dose of 3 g daily. The maximal effect of the medication is achieved 4-6 hours after taking it, and it takes 10-12 hours before the kidneys excrete it7. A long-term follow-up study of infants born to women treated with methyldopa during pregnancy found no increased incidence of general health or mental health problems. In addition, methyldopa can be combined with other antihypertensives to achieve the desired blood pressure target[27].

Both nifedipine and amlodipine are more often used as therapy if the patient's clinical condition has a blood pressure of more than 160/110 mmHg; the results of this study are consistent with the 2016 Indonesia Society of Obstetricians and Gynecologist reference standard, which states that the CCB group is used if the patient's blood pressure is more than 160/110 mmHg. Peroral administration of nifedipine for pre-eclampsia patients is usually given at a dose of 20-30 mg/ day 2-3 times per day; nifedipine at this dose can reduce blood pressure in pre-eclampsia patients.

Giving nifedipine for 2-5 days can reduce blood pressure. Nifedipine has a short mechanism of action that increases the frequency, intensity, and duration of angina pectoris associated with acute hypotension[7]. Nifedipine is fast-acting within 10-20 minutes after oral administration with fewer side effects, so it is often used prenatally. Very little calcium channel blocker is excreted in an intact form via the kidneys, so there is no need for dose adjustment in patients with impaired renal function. The main side effect of nifedipine is due to excessive vasodilation. Symptoms observed include dizziness or headache due to meningeal artery dilatation, hypotension, reflex tachycardia, facial flushing, nausea, vomiting, peripheral edema, cough, and pulmonary edema[28]. Amlodipine, with a dose between 2.5 to 10 mg, can be given once a day because it has a long half-life. A once-daily dose can reduce blood pressure that lasts for 24 hours. Administration of amlodipine does not cause acute hypotension because the onset of action of amlodipine is slow[29].

CONCLUSION

The antihypertensive medications used in preeclampsia patients in several public and private hospitals in Banyumas were α2-adrenergic agonist group, namely methyldopa by 52.8% and Calcium Channel Blocker (CCB) group, namely nifedipine by 45.2 % and amlodipine by 2 %. The rationality of medication used in preeclampsia patients in public and private hospitals in Banyumas obtained from indicators such as right patient, suitable indication, proper medication, right dose, and right route of administering the medication were 100%. The effectiveness of therapy in preeclampsia patients can reduce patient blood pressure, with an average decrease in systolic pressure by 37 mmHg, an average decrease in diastolic pressure by 22 mmHg and an average decrease in MAP by 28 mmHg.

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