ISSN 2745-455X (Online)
Indonesian Journal of Pharmacology and Therapy

Evaluation of administration and use of antihypertensive drugs in severe preeclampsia patients at X General Hospital in Jakarta

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https://doi.org/10.22146/ijpther.1347

Submitted: 21/02/2021
Accepted : 23/06/2021

Keywords:
preeclampsia,
hypertension,
adherence,
therapeutic,
guideline,
maternal mortality,

ABSTRACT

The high number of maternal mortality rate (MMR) is still a problem in Indonesia. Three ethyologies of maternal death are infection (12%), hypertension in pregnancy (25%) and bleeding (30%). Pre-eclampsia as a form of hypertension during pregnancy requires antihypertensive drug therapy. Rationality assessment for any kinds of pharmacotherapy is based on the right indication, the right medicine, the right patient, and the right dose. The main indication for antihypertensive medication in pregnancy is applied to the mother's in preventing cerebrovascular disease. The aim of this study was to evaluate the characteristics, patterns and accuracy of the administration and use of antihypertensive drugs in patients with severe preeclampsia at X General Hospital in Jakarta in 2018. It was a non-experimental study with a descriptive and retrospective design using medical records. Administration and use of antihypertensive drugs in patients with severe preeclampsia at the X General Hospital in Jakarta showed 91.9% right indication, 86.72% right drug, 96.9% right patient and only 5.26% right dose with 4.0% accuracy of rational administration and use of drugs. In conclusion, the right dose in the management of patients with severe preeclampsia in X General Hospital in Jakarta is still low. Further training and close monitoring and evaluation on the rational use of antihypertension in severe preeclampsia is needed.

ABSTRAK

Angka kematian ibu (AKI) yang tinggi masih menjadi suatu masalah kesehatan yang perlu diperhatikan di Indonesia. Tiga penyebab utama dari kematian ibu adalah infeksi (12%), hipertensi dalam kehamilan (25%), dan perdarahan (30%). Pre-eklampsia dapat dikatakan sebagai salah satu bentuk hipertensi pada saat kehamilan yang memerlukan terapi obat antihipertensi. Penilaian rasionalitas berdasarkan tepat indikasi, tepat obat, tepat pasien, dan tepat dosis. Indikasi utama pemberian obat antihipertensi pada kehamilan adalah untuk keselamatan ibu dalam mencegah penyakit serebrovaskular. Tujuan penelitian ini untuk mengetahui karakteristik, pola penggunaan dan ketepatan pemberian serta penggunaan obat antihipertensi pada pasien preeklampsia berat di Rumah Sakit Umum X di Jakarta tahun 2018. Penelitian ini merupakan jenis penelitian non eksperimental dengan desain deskriptif, retrospektif dengan menggunakan rekam medik. Persentase pemberian dan penggunaan obat antihipertensi pada pasien preeklampsia berat di RSUP X di Jakarta menunjukan 91,9% tepat indikasi, 86,72% tepat obat, 96,9% tepat pasien dan 5,26% tepat dosis dengan persentase ketepatan pemberian dan penggunaan obat rasional sejumlah 4,0%. Dapat disimpulkan, ketepatan dosis dalam pengelolaan pasien preeklampsia berat di Rumah Sakit Umum X di Jakarta masih rendah. Perlu pelatihan lebih lanjut dan pengawasan serta evaluasi yang ketat dalam penggunaan antihipertensi yang rasional pada preeklamsia.

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INTRODUCTION

The high number of maternal mortality rate (MMR) is still a health problem that needs to be seriously considered in Indonesia. The MMR can show the quality of health services during pregnancy and pregnancy. The three main causes of maternal death are infection (12%), hypertension in pregnancy (25%) and bleeding (30%).[1] Based on 2015 Inter-Census Population Survey (SUPAS) data, the MMR for Indonesia decreased gradually from 346 deaths per 100,000 live births in 2010 to 305 death per 100,000 live births.[2] However, this figure still under the MDG target in 2015 of 102 per 100,000 live births.

According to the Queensland Clinical Guideline (2015) preeclampsia is defined as hypertension that occurs after 20 weeks of pregnancy, confirmed after 2 times or more examinations and accompanied by disorders of one or more organs/organ systems. This symptom is often accompanied by proteinuria. Pre-eclampsia is divided into mild/moderate pre-eclampsia with blood pressure ≥140-159/90-109 mmHg and severe pre-eclampsia with blood pressure ≥ 160/110 mmHg.[3] Pre-eclampsia in pregnancy not only impacts during pregnancy and childbirth, but also causes postpartum problems due to endothelial dysfunction in various organs so it manifests towards more serious complications.[4]

The aim of this study was to determine the characteristics, patterns and accuracy of the administration and use of antihypertensive drugs in patients with severe preeclampsia at the X General Hospital Jakarta in accordance to the guidelines approved by the Indonesian Association of Obstetrics and Gynecology (*Perkumpulan Obstetri dan Ginekologi Indonesia*/POGI).[1]

MATERIALS AND METHODS

Subjects

This was a retrospective study using medical records obtained from X General Hospital in Jakarta. Data of cases were extracted from existing medical record from January-December 2018. The inclusion criteria were patients with severe preeclampsia, whereas the exclusion criteria was severe preeclampsia patients who did not have complete medical record. The number of samples needed for the study, after being calculated, was 123 cases. Protocol of the study was approved by the Research Ethics Committee of the X General Hospital Jakarta with ref. no. 84/KEPK-RSUPP/12/2019.

Protocol of study

One hundred and twenty-three cases that met the inclusion and exclusion criteria were administratively selected and involved in this study. The cases were then evaluated and categorized into 4 categories namely precise indications, precise medications, appropriate patients and appropriate dosages. The drug use was considered rational when the prescription is in accordance with the needs and conditions of the patients in an adequate period of time and at the lowest price for the patient and the public at large, as highlighted in the guideline.[1]

Data analysis

Data were presented as frequency and percentage and then descriptively analyzed.

RESULTS

As much as 182 cases from medical records from January-December 2018 were selected. However, only 123 cases that met the inclusion and exclusion criteria to be analyzed (FIGURE 1).

The demographic characteristics of patients are presented in TABLE 1. The largest distribution of age range of patients who suffering severe preeclampsia was of 20-35 years with a total of 82 (66.7%) patients and the smallest distribution of age was <20 years with a total of 4 (3.3%) patients.

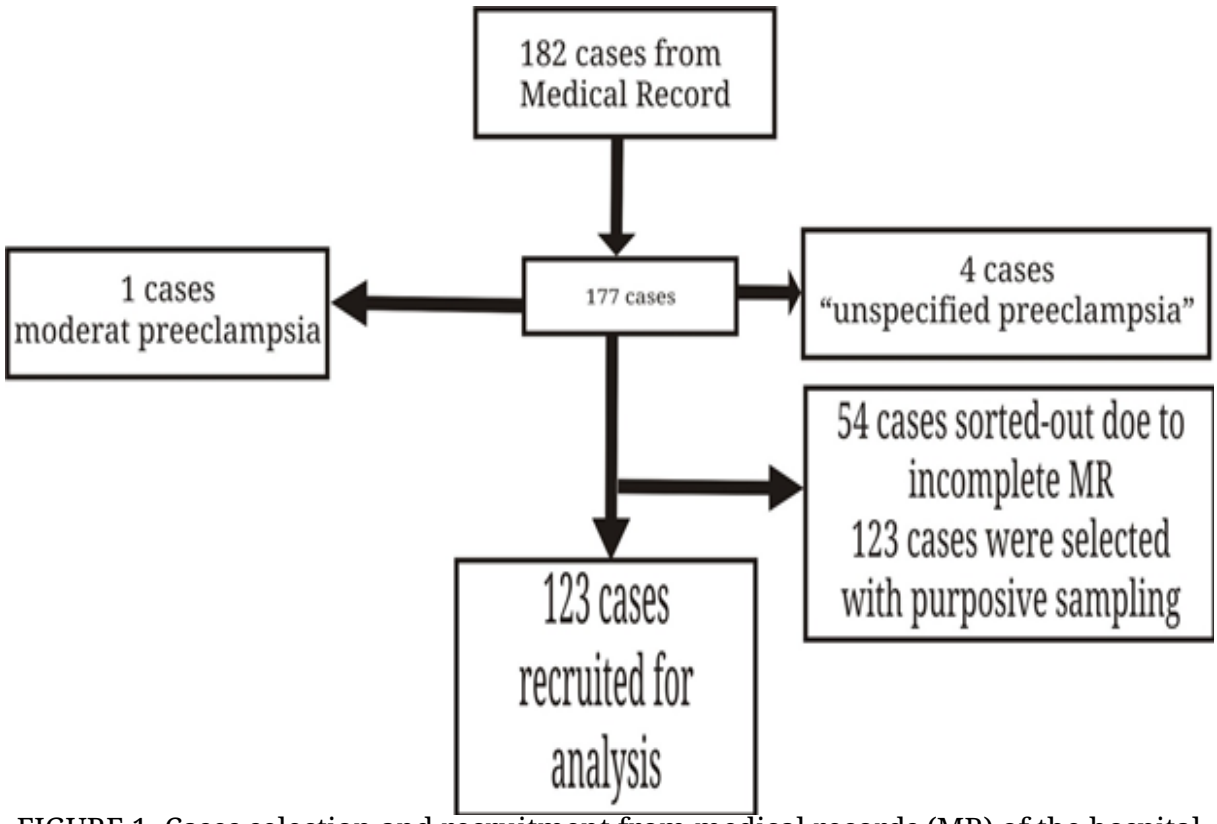

FIGURE 1. Cases selection and recruitment from medical records (MR) of the hospital

TABLE 1. Demographic characteristics of patients

Characteristics	Number of patients [n (%)]
Age (years old)	
• <20	4 (3.3)
• 20-35	82 (66.7)
• >35	37 (30.1)
Pregnancy period	
• Trimester II	1 (0.8)
• Trimester III	122 (99.3)
History of preeclampsia	
• Yes	15 (12.2)
• Never	108 (87.8)
Marriage status	
• Married 1x	115 (93.5)
• Married >1x	8 (6.5)
Other history of diseases	
• Yes	37 (30.1)
• None	86 (69.9)
Total	123 (100)

Previous and present of diseases accompanied of severe preeclampsia patients are presented in TABLE 2. Previous hypertension was risk factors for preeclampsia in this study. Severe preeclampsia suffered by 16 patients who previous suffered hypertension and only one patients who had recent hypertension. TABLE 3 shows anti-hypertension used in patients with severe preeclampsia. Nifedipine was the most antihypertensive drug used in severe preeclampsia patients. Nifedipine single drug was administered to 95 (77.2%) severe preeclampsia patients in this study. Nifedipine also was administered in combination with other one or two other antihypertension drugs.

Rationality of antihypertensive use prescribing to severe preeclampsia patients is presented in TABLE 4. The right indication, right drug and right patients were relatively high (> 86%). However, the right dosage and percentage were relatively low (≤ 5.3%).

TABLE 2. Previous and present of diseases of patients

Present disease	[n (%)]	Previous diseases	[n (%)]	History of allergy	[n (%)]
Hypertension	1 (0.8)	Hypertension	16 (13)	Allergy	8 (6.5)
Kidney	2 (1.6)	-	-	No	115 (93.5)
Diabetes	3 (2.4)	Diabetes	4 (3.3)	-	-
Obesity	4 (3.3)	-	-	-	-
Heart disease	1 (0.8)	Heart disease	1 (0.8)	-	-
Others	2 (1.6)	Others	3 (2.4)	-	-
None	110 (89.4)	None	99 (80.5)	-	-
Total	123 (100)	-	123 (100)	-	123

TABLE 3. Distribution of anti-hypertension used in patients with severe preeclampsia

Anti-hypertension	[n (%)]
Monotherapy	
• Nifedipine	95 (77.2)
• Methyldopa	7 (5.70)
• Propranolol	1 (0.8)
• Ramipril	1 (0.8)
Combination (two drugs)	
• Nifedipine + methyldopa	9 (7.3)
• Nifedipine + captopril	1 (0.8)
• Nifedipine + micardis (telmisartan)	1 (0.8)
• Nifedipine + propranolol	1 (0.8)
Combination (three drugs)	
• Nifedipine, methyldopa and captopril	2 (1.6)
Not receiving any drugs	5 (4.1)
Total	123 (100)

TABLE 4. Accuracy (%) of administration and use of antihypertensive drugs at X General Hospital

Criteria	Right	Not right
	[n (%)]	[n (%)]
Right indication	113 (91.9)	10 (8.1)
Right drug	98 (86.7)	15 (13.2)
Right patient	95 (96.9)	3 (3.0)
Right dosage	5 (5.3)	90 (94.7)
Right percentage	5 (4.0)	-

DISCUSSION

The largest distribution of age range of patients who suffering severe preeclampsia was of 20-35 years with a total of 82 (66.7%) patients and the smallest distribution of age was <20 years with a total of 4 (3.3%) patients TABLE 1. This result is in accordance with the result reported by Sumampouw *et al.*[5] who stated that the number of ages suffering severe preeclampsia ranged 20-35 years. Productive period for a woman to plan a pregnancy ages 20-35 years. The productive period is associated to the high incidence of preeclampsia due to high work load and physical activity which trigger stress of the mother.

Pregnancies with history of hypertension was risk factors for preeclampsia in this study. Severe preeclampsia suffered by 16 patients who previous suffered hypertension and only one patients who had recent hypertension (TABLE 2). Women who want to get pregnant and has hypertension, their blood pressure should be well-controlled, and should be well assessed from the first Ante-Natal-Care (ANC) visit.[6]

Diagnosis of severe preeclampsia was conducted base on the criteria of POGI's Guideline, 2016.[1] A patients is considered as severe preeclampsia if >20 weeks gestation with the presence of one or more symptoms such as systolic blood pressure value ≥160 mmHg or diastolic ≥110 mmHg, or the value of proteinuria ≥ 5g/24 hours or ≥ +2 dipstick, or the presence of other organ disorders such as thrombocytopenia (<100,000/uL), microangiopathic hemolysis, increased SGOT and SGPT, epigastric pain or upper right quadrant, persistent headache, vision scotoma, stunted fetal growth, oligohydramnios, pulmonary edema, congestive heart failure, oliguria (≤ 500 mL/24 hours), creatinine ≥ 1.2 mg/dL. Based on the POGI's Guideline 2016, 113 patients (91.9%) involved in this study fall into the indication criteria (TABLE 4). However, Sari *et al.* (2018) obtained the results of accuracy indications by 100% based on the accuracy of diagnosis judging by the value of blood pressure and patients who received antihypertensive drug.[7] In this study, however, there were 10 patients that fall into incorrect indications because some patients did not match the diagnosis of severe preeclampsia, while the rest have to be done termination because they have ruptured amniotic.

The rational antihypertension use in this study showed 98 patients (86.72%) were given appropriate drugs, while as many as 15 patients (13.2%) were not given the appropriate drugs (TABLE 4). This result is not much different from the research conducted by Amri (2015) who got the right results of drugs with 48 cases (81.35%) and improper drug 11 cases (18.64%).[8] POGI's guideline recommends the use of antihypertension such as nifedipine, nicardipine, atenolol and methyldopa only. However it does not recommend the presence of combination therapy given to patients with hypertension in pregnancy. There were 15 cases of inaccurate treatment,

consisting of 1 patient given ramipril, 1 patient propranolol and 12 patients a combination of two types of drugs namely methyldopa + nifedipine (9 patients), nifedipine + captopril (1 patient), nifedipine + micardis (1 patient) and nifedipine + propranolol (1 patient). In addition, there are 2 patients who received a combination of three types of drugs namely nifedipine + methyldopa + captopril.

There were 3 patients who were categorized as incorrect patients i.e. one patient given nifedipine and two patients given methyldopa. One patient with a history of heart disease was given nifedipine. It is a calcium channel blocker that inhibits calcium from entering cells resulting in vasodilation of blood vessels of the heart muscle leading to lower blood pressure. Actually, severe preeclampsia is related to impaired myocardial and endomyocardial function. Nifedipine with its cardio-protectant property may be advantageous for severe preeclampsia patients. However, nifedipne is contraindicated to patients who allergy to nifedipine, having acute myocardial infarction, angina and cardiogenic shock. Therefore, the administration of this antihypertensive in patients with a history of heart disease is not recommended.[9] Two patients with history of anemia and given methyldopa can cause depression, orthostatic hypotension and dizziness more often than other antihypertensive drugs, even hemolytic anemia. Therefore, methyldopa should not be given for patients with history of anemia.

The accuracy was determined based on the amount, duration, frequency and route of drug administration recommended by POGI's Guideline 2016.[1] The results showed only 5 patients (5.26%) were given the right dose, while 90 patients (94.7%) were classified in the inappropriate dosage. They were given 4 x 10 mg/day which not in accordance with the guideline. This results differ greatly from the study conducted by Andriana *et al.*[10] who reported that 68 patients (100%) were classified as the right dose category. The POGI's Guideline recommended that nifedipine is administered in 10 mg oral capsule dosage, repeated every 15 -30 min, with a maximum of 30 mg, in other words the recommended dose is 3 x10 mg/day. Excessive use of calcium channel blocker can cause hypotension leading to fetal hypoxia and acidosis.

The recommended dosage for methyldopa is 250-500 mg orally 2 or 3 times a day, with a maximum dose of 3g per day. In a hypertensive crisis with systolic blood pressure >200 mmHg or diastolic> 120 mmHg, IV methyldopa 250-500 mg can be given every 6 hrs up to a maximum of 1 g every 6 hrs as an alternative of antihypertensive therapy without using combination drug therapy.

We found no data related to the use of MgSO4 for the prevention of preeclampsia or preventing the degree of preeclampsia from mild or moderate to severe, as well as to prevent the occurrence of eclampsia, although the use of MgSO4 is not for all cases of preeclampsia.[11] The difference in results in this study may be due to differences in the use of guidelines at the X General Hospital.

CONCLUSION

In conclusion, the right indication, right drug and right patients are relatively high in the management of patients with severe preeclampsia in X General Hospital in Jakarta. However, the right dosage and percentage were relatively low. Continuous training for doctors and midwives who involved in the management of severe preeclampsia are needed, furthermore close monitoring by doctors should be encouraged.

ACKNOWLEDGEMENT

Authors would like to thank the Head of Department of Obstetric Gynecology, X General Hospital for support this study.

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