

Problems in managing eclampsia

John Wantania

Department of Obstetrics Gynecology Medical Faculty of Sam Ratulangi University/

Prof. Dr. R. D. Kandou Hospital Manado

Email: john_w_md@yahoo.com

Abstrak: Eklamsia masih merupakan masalah penting akibat tingginya morbiditas dan mortalitas. Penanganan yang tertunda biasanya berawal dari deteksi dan rujukan yang terlambat akibat variasi karakteristik yang luas dari preeklamsia dan terdapatnya berbagai teori mengenai patomekanismenya. Masalah tambahan sering menyertai terminasi kehamilan, pemakaian obat antikonvulsan dan antihipertensi, keluaran perinatal, dan *follow-up* pasca kelahiran. Penanganan eklamsia yang kompleks memerlukan penatalaksanaan yang komprehensif dan terintegrasi.

Kata kunci: penanganan eklamsia, masalah

Abstract: Eclampsia is still an important problem due to its high morbidity & mortality. Delayed management usually starts from late detection and referring due to the wide characteristic variation of preeclampsia and various pathomechanism theories. Additional problems often associated with termination of pregnancy, use of anticonvulsant and antihypertensive drugs, perinatal outcome, as well as post partum follow-up. Managing eclampsia is still complicated and needs a comprehensive and integrative management.

Keywords: managing eclampsia, problems

To date, eclampsia remains as one of the main causes of maternal and fetal morbidity as well as mortality. Based on WHO data, eclampsia causes maternal mortality by 12% in developing countries.¹ Data of Indonesia in WHO showed that maternal mortality ratio (MMR) in 2013 was 190 per 100,000 live births.² More than 25% maternal deaths occurred in Indonesia in 2013 were caused by hypertension in pregnancy.³ According to Sahin,⁴ MMR due to eclampsia ranged from 1.8% (UK) to 6.1% (Colombia).

The causes of eclampsia (or preeclampsia) are still not fully understood. Although many pathomechanism theories try to explain it but the management and prognosis have not undergone many changes.⁵ The main characteristics of preeclampsia are hypertension and proteinuria, whereas in eclampsia, seizure or coma

occur.⁶ In addition to blood pressure, proteinuria is also used as a marker to distinguish degrees of preeclampsia.¹ Albeit, when it is associated with complications or outcome of preeclampsia, proteinuria is considered as a poor predictor.^{7,8} In patients with eclampsia, proteinuria >3+ is associated with significant perinatal mortality rate.⁹

Current techniques, such as the protein to creatinine ratio, may become a more accurate alternative. In high possibility of false positive, the 24-hour urine is recommended for examination of significant proteinuria unless delivery is immediately terminated. However, complications of preeclampsia may occur in the absence or prior to proteinuria.^{10,11} In fulminating preeclampsia, progressive development can also suddenly occur regardless of the degree of preeclampsia.

Avoidable factors

Preeclampsia detection in community

Given that many problems occur in preeclampsia-eclampsia, in addition to explore the pathomechanisms of preeclampsia-eclampsia, recent studies also tried to find markers that could be predictors or related to the prevention and prognosis. Although there are numbers of potential markers for prediction of pre-eclampsia, there is still some inconsistency between studies. Preeclampsia is a multi-factorial condition that requires a combination of several markers, with a vague future, moreover, being used as a routine and affordable marker.^{12,13}

Milne et al.¹⁴ suggested a form of practical recommendations:

1. Risk assessment in early pregnancy, namely the identification of pre-eclampsia predisposing factors, as follows: first pregnancy, preeclampsia history, birth interval ≥ 10 years, age ≥ 40 years, BMI ≥ 35 , preeclampsia family history (mother or sister), early diastolic pressure ≥ 80 mmHg, initial proteinuria $\geq +$, twin pregnancy, and history of medical disorders/diseases (hypertension, renal disease, diabetes mellitus, antiphospholipid syndrome)
2. Refer in early pregnancy. In pregnancies with a history of preeclampsia, twin pregnancy, presence of accompanying diseases, or if there are more than two factors, it is advisable to refer before 20 weeks gestation to a specialist level.
3. Monitoring after 20 weeks of gestation: newly occurred hypertension or proteinuria, symptoms of headache or blurred vision, vomiting and epigastric pain, and reduction of fetal movement or intrauterine growth restriction (IUGR)

Provision of low-dose aspirin and calcium supplementation are still recommended by some experts, especially at high risk preeclampsia and early onset, although there is still controversial, therefore, it requires a tight monitoring.⁸

Preeclampsia problem in developing countries

Preeclampsia in developing countries typically starts in areas far from health centers with the condition of society which is generally classified as low socio-economic, therefore, the problems often become much more complex. Generally speaking, there are four delays, namely: delay in knowing early signs of danger/problems/risk factors; delay in decision making; delay in transportation; and delay in management at the referral site.¹⁵

In developing countries, particularly Indonesia, the delays are mainly caused by geographic, social, and cultural factors as well as social and economic traps.¹⁵ Geographic factor is associated with remote areas and distant islands which are far from health facilities and access to referral sites. Social and cultural factors occur in the community who have traditional beliefs, and so the utilization of health manpower and health care facilities is not optimal. Meanwhile, social and economic traps are related to financial problems.

On the other hand, eclampsia should be at least treated at the tertiary hospital with specialized level. Besides of problems in the facilities/equipment and adequacy of staff, emergency referral system should have good auditing system.^{10,16,17}

Identifying the problems

Differential diagnosis

Eclampsia is often distinguished by numbers of other conditions such as epilepsy, tetanus, meningitis, and septicemia.¹ In Indonesia, especially in regions such as North Sulawesi, malaria (including malaria in pregnancy) is still a serious problem; therefore, it is important to differentiate severe (cerebral) malaria from eclampsia.

In addition to the differential diagnosis, there are often several limitations to diagnose conditions that require further laboratory examinations such as HELLP syndrome.

Impending/imminent eclampsia

Symptoms of blurred vision, headaches and heartburn which are included as criteria for severe preeclampsia, are also signs of impending eclampsia. Nevertheless, some women may develop eclampsia without prodromal signs. Diagnosis of impending eclampsia or eclampsia usually refers to the conditions requiring termination of pregnancy.^{10,11}

Eclampsia at preterm gestational age

Treatment of preeclampsia is labor and delivery of the placenta.¹⁸ Albeit, the severe preeclampsia can still be considered for conservative treatment/expectative management in preterm pregnancy.¹⁹ In early preeclampsia (early onset), only half of which could undergo expectative management, while the rest is mainly associated with fetal distress or maternal complications soon after stabilization and evaluation.²⁰ In expectative management, in addition to monitoring staff, the availability of Doppler facilities and cardiotocography are the best monitoring methods associated with time of termination.²¹

Kidanto et al.¹⁷ found that antepartum eclampsia was 47% of all eclampsia cases, and mostly (70%) occurred at preterm gestation. It causes problematic consequences associated with the termination of pregnancy versus the viability of the fetus, although ultimately the maternal factors become the priority. In addition to eclampsia, maternal complications that can occur and require monitoring since the beginning including solutio placenta, HELLP syndrome, uncontrolled hypertension, pulmonary edema, and cerebrovascular accident.²¹

In South Africa, the overall hypertension in pregnancy contributed up to 39% of perinatal deaths, most occurred in babies with birth weight <2000 g (preterm and IUGR); and only 9% of neonatal deaths occurred in babies with birth weight >2000 gram. Infant respiratory distress syndrome (IRDS) was responsible for 23% of neonatal deaths, but the greatest mortality occurred before birth.²¹

Infant morbidity depends on the gestation age at the time of birth and the use of corticosteroid therapy, if given, thereby increasing the baby's lung maturity. Corticosteroids may be useful even though the labor is less than 24 hours.¹⁰

Pregnancy termination

Selection of delivery usually depends on obstetric indications and patient's condition. Labor must be performed immediately after the patient's condition is stable.^{10,11} In a study in Faisalabad, the morbidity and mortality were lower in patients with vaginal delivery compared with cesarean section.²²

Of course, this will be more successful in certain circumstances such as high Bishop score or multigravida. Induction of labor can be done immediately if the patient has been stabilized and there are no obstetric contraindications. Caesarean delivery can be an option for women with unfavorable cervical conditions or gestational age ≤ 30 weeks since induction in women with such situation cause long labor, therefore, the risk of complications will increase.^{10,11}

Managing eclampsia***Anticonvulsants***

Magnesium sulfate has proven its effectiveness in prevention and management of eclampsia. In terms of cost, it is affordable to be used in developing countries. Some studies have shown its advantages compared to diazepam and phenytoin.^{23,24} In Sharma's study²⁵ with the use of phenytoin, there were cases of severe preeclampsia developing eclampsia while the incidence of recurrent eclampsia occurred in six patients (24%).

The use of diazepam should be noted that there are possibilities of infant respiratory depression, which usually can occur at doses more than 30 mg in 1 hour. Though relatively safe for the mother and the baby, in providing magnesium sulfate, we must notice the variety of standard guidelines, supervision, antidotum availability, and recurrent seizures, although the possibilities are relatively low.^{1,6}

Antihypertensive drugs

Hypertension management does not cure preeclampsia, and further aims to prevent cerebral haemorrhage and eclampsia as well as to delay proteinuria. Antihypertensive drugs should be given to all pregnant women with systolic blood pressure higher than 160-170 mmHg or diastolic blood pressure higher than 110 mmHg. A number of drugs used to control severe hypertension are *inter alia* nifedipine, labetalol, and hydralazine. Management of mild hypertension (systolic blood pressure 140-160 mmHg or diastolic blood pressure 90-100 mmHg) is still controversial, yet some physicians still provides therapy, especially in severe proteinuria and liver or hematological disorders.^{8,10,11,26}

Drugs that are considered safe and effective are often used as first-line therapies *inter alia* methyldopa *i.e.*, labetalol and oxprenolol. ACE inhibitors and angiotensin receptor blockers are contraindicated in pregnancy because they can cause kidney damage, while diuretics should be avoided except in special conditions such as pulmonary edema.^{8,10,11,26} Hydralazine has more tendencies to cause maternal hypotension, cesarean section, placenta previa, oliguria, impaired fetal heart sound, and low Apgar score at the first minutes.^{26,27} Atenolol should be avoided in pregnancies because it can cause IUGR, whereas labetalol should be avoided in patients with asthma.^{10,11}

In addition to anticonvulsant agents, antihypertensive selection is also important. The selection of safe medication, monitoring side effects, even the availability of drugs can often cause problems. In some places in Indonesia, for example, labetalol and hydralazine are hard to find, the use of drugs like clonidine, which can cause rebound phenomenon, are increased in the guidelines. Besides nifedipine, nicardipine, another calcium channel blocker, can be used parenteral and will be effective after 10-20 minutes.⁶ The use of other new drugs are still in research.

Perinatal outcome

Although fetal survival during preeclampsia pregnancy undergoes many changes, probably due to more aggressive treatment, on the other hand, neonatal mortality has not undergone many changes. In eclampsia, stillbirth, prematurity, and asphyxia are conditions associated with perinatal death. Birth interval >12 hours after seizure, diastolic blood pressure >110 mmHg, and proteinuria >3+ show a high perinatal mortality. Early referral strategy, early resuscitation, and early neonatal service are expected to improve the quality of existing outcome.⁹

Immediate termination of pregnancy reduces the risk of a stillborn baby because it reduces the length of the critical period in the baby.⁹

Postpartum eclampsia

Eclampsia can occur during antepartum, intrapartum, or postpartum in more than 30% of cases.²⁹ The majority of postpartum eclampsia occurs at full term pregnancy.^{10,17}

Late postpartum eclampsia (LPE) has onset within 48 hours of childbirth up to four weeks postpartum. LPE can occur without prodromal symptoms of preeclampsia, including proteinuria. However, adequate evaluation and reported symptoms of preeclampsia, namely headache and visual impairment, could reduce mortality associated with childbirth. Slow onset and atypical presentation may cause diagnostic errors.^{11,30}

Follow-up

Possibility of postpartum eclampsia must still be considered primarily from aterm pregnancy where this risk begins to decline after four days post partum which is the minimum limit of treatment in patients with good clinical condition.¹⁰

Fluid restriction during intrapartum and postpartum is more related to the prevention of lung edema, and fluid restriction 80 ml/hour or 1 cc/kg/h unless maternal hemorrhage occurs.¹⁰ Fluid restriction during pregnancy can cause fetal

hypoxemia in epidural analgesia and administration of magnesium sulphate can cause mediate vasodilation.¹¹

Most patients with preeclampsia (13%) can develop into chronic hypertension. Antihypertensive drugs should be continued in the intrapartum and postpartum periods. In some cases, blood pressure may take up to three months to return to normal, and blood pressure should be maintained not to exceed 160/110 mmHg. Alpha methyl dopa can cause postpartum depression. In breastfeeding women, labetalol, atenolol, nifedipine, and enalapril may be used as a single drug or in combination.¹⁰

Conclusion

Eclampsia is still a challenging problem due to its high morbidity and mortality. Managing eclampsia is complicated and needs a comprehensive and integrative management.

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