Original Article

A 13-Year Review of Eclampsia and Anesthetic Techniques at a Single Tertiary Care Center

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Objective: To assess recent perinatal outcomes of women with eclampsia in relation with the choices of anesthesia.

Materials and Methods: The electronic medical records of women with eclampsia that delivered at a single tertiary care center between January 2005 and December 2017 were retrospectively reviewed. Anesthesiologists had the discretion to decide the choice of anesthesia for cesarean delivery.

Results: The authors identified 45 eclampsia cases from 113,914 deliveries during the study period. The mean ± standard deviation (SD) of maternal age and gestational age at delivery of the cases was 24.4±8.5 years and 35.4±3.0 weeks, respectively, and 32 (71.1%) were primigravids. There were 29 (64.4%), eight (17.8%), and eight (17.8%) eclampsia cases that occurred antepartum, intrapartum, and postpartum, respectively. Out of the cohort, 35 (77.8%) underwent Cesarean delivery, of which 18 (51.4%) and 17 (48.6%) received general anesthesia or combined, and regional anesthesia, respectively. There was one (2.2%) maternal and three (6.67%) neonatal deaths. The general anesthesia group had a higher incidence of platelets of less than 100,000/mL and higher admission to the intensive care unit ($p<0.05$).

Conclusion: Eclampsia remains a cause of serious perinatal morbidity. Most eclampsia occurred without prior risks, warning signs, or a critically high blood pressure. With proper patient selection and individualization, general or regional anesthesia is safe. The higher intensive care unit admissions were likely attributable to severe sequelae of eclampsia in those that underwent a general anesthesia.

Keywords: Eclampsia, General anesthesia, Spinal anesthesia, Epidural anesthesia, Perinatal outcomes

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Eclampsia is a rare but serious complication of pregnancy[1,2]. It is defined as generalized convulsions or coma co-existing with pre-eclampsia and not attributable to any other causes during pregnancy or postpartum. Definitive treatment of eclampsia is timely delivery, although the patient may seize before, during or after delivery[3]. Eclampsia is responsible for 10% of maternal deaths and is the major cause of admission to intensive care unit (ICU) after delivery[4]. Operative delivery such as vacuum, forceps, and cesarean deliveries, and complications from anesthesia can further increase perinatal morbidities. Anesthesiologists have a major role in preoperative medical assessment and optimization of the patient such as airway and blood pressure management, control and prevent further convulsion, and give the most proper choice of anesthesia for termination of pregnancy.

Obstetric patients are already at a higher risk for general anesthesia (GA) and regional anesthesia (RA)[5]. Administering a GA is particularly a challenge in pregnant women because of the physiological changes they undergo, leading to a potentially difficult airway and failed intubation, and the risk of aspiration pneumonitis. Women with pre-eclampsia-eclampsia need additional precautions for thrombocytopenia. In addition, anesthetists need to be alert for a potential aggravated hypertensive response to laryngoscopy and intubation, resulting in intracranial hemorrhage with possible drug interactions between magnesium sulfate ($MgSO_4$) and non-depolarizing muscle relaxants[6,7]. The RA may be a safer option in low-risk obstetric patients, but the procedure may be more challenging in eclampsia cases with profound thrombocytopenia, and in those who are unable

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Table 1. Diagnostic criteria for pre-eclampsia/eclampsia and corroborative management at the Faculty of Medicine Siriraj Hospital

Diagnosis	Criteria
Preeclampsia (prior to November 2013)[15]	- De novo hypertension (SBP ≥140 mmHg or DBP ≥90 mmHg) after 20 weeks of gestation, and - Proteinuria 1+ dipstick (30 mg/dL)
Preeclampsia (from November 2013)[16]	- De novo hypertension (SBP ≥140 mmHg or DBP ≥90 mmHg) after 20 weeks of gestation, and - Proteinuria 1+ dipstick (30 mg/dL), or - Headache, visual change, scotoma - Pulmonary edema - Platelets <100,000/mL - Elevated serum creatinine 2x or >1.1 mg/dL - Elevated AST/ALT 2x or >70 IU/L
Eclampsia[16]	Seizure or coma that cannot be attributed to other causes in women with preeclampsia

SBP=systolic blood pressure; DBP=diastolic blood pressure; AST=aspartate aminotransferase; ALT=alanine aminotransferase

to cooperate. Transplacental passage of anesthetic agents during GA, and severe maternal hypotension during RA due to pre-eclampsia-related contraction of intravascular volume, increase the risk of neonatal depression as reflected by persistently low Apgar scores.

There have been numerous publications on the anesthetic management of women with pre-eclampsia, including the present study[8-12]. Despite this, there is a paucity of published data on the optimal management of these cases. This is due to a significantly decreased incidence of pre-eclampsia in modern obstetrics as a result of increased use of magnesium sulfate ($MgSO_4$) to manage it[1,13]. In the current study, the authors aimed to review the recent nature and perinatal outcomes of women with eclampsia in relation to the choice of anesthesia, after implementation of the institutional guidelines for diagnosis and management of pre-eclampsia-eclampsia[14].

Materials and Methods

The authors retrospectively analyzed eclampsia cases from an electronic medical record (EMRs), reviewing women who delivered in the Department of Obstetrics and Gynecology, Faculty of Medicine Siriraj Hospital, between January 2005 and December 2017. This period corresponded with the implementation of the authors institutional guidelines for diagnosis and management of pre-eclampsia-eclampsia in 2004[14]. Ethical approval was obtained from the Siriraj Institutional Review Board (SIRB 390/2017), and the study had been registered with www.ClinicalTrials.gov (NCT04160923).

Eclampsia was defined as the occurrence of one or more generalized convulsions[1], or coma in the setting of pre-eclampsia[2], and the convulsions are not attributable to any other causes[3]. Definitions of pre-eclampsia or eclampsia are summarized in Table 1. As per the authors' 2004 institutional guidelines for the diagnosis and management of pre-eclampsia or eclampsia, first-line therapy for seizure control is intravenous $MgSO_4$. For the management of blood pressure, the authors' first-line treatment was hydralazine, labetalol, or nifedipine, with nitroglycerine or sodium nitroprusside as second-line medications[13,14]. Prompt delivery was conducted after controlling the seizures and stabilizing the patients' vital signs. Vaginal delivery was conducted if the cervix was ready. The choice of anesthesia for Cesarean delivery, GA with endotracheal intubation, or RA as spinal or epidural anesthesia, depended on the patient's condition. A platelet count of less than 100,000/mL was a contraindication for RA. The present study rationales, indications, and protocols for general, spinal, and epidural anesthesia for Cesarean delivery are shown in Table 2.

Diagnoses and procedures, including routes of delivery, were coded using the Tenth Revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10), and the Nineth Revision of the International Statistical Classification of Diseases, Clinical Modification (ICD-9-CM). The EMRs with codes O14 and O15 were identified, and manually reviewed by two investigators (Wongsripuemtet P and Khumchoei C) to confirm the diagnosis of eclampsia. Clinical details and perinatal outcomes of all the cases were extracted and analyzed for possible correlations with the choice of anesthetic method.

Statistical analysis

Continuous data with parametric distribution were presented as descriptive statistics using percentage (%) and mean ± standard deviation (SD). Continuous data with non-parametric distribution were presented as median with (minimum, maximum)

Table 2. Rationales, indications, and protocols for general, spinal, and epidural anesthesia for Cesarean delivery at Faculty of Medicine Siriraj Hospital[17]

	General anesthesia	Spinal anesthesia	Epidural anesthesia
Rationales: pros	- Fast - Better control of blood pressure	- Better control of postoperative pain	- Better control of postoperative pain - Can be supplement during surgery and for continuous infusion
Rationale: cons	- Difficult airway, failed intubation, and hypoxemia (due to edema of the airway, especially in women with preeclampsia) - Hypertension during airway manipulation can precipitate intracranial hemorrhage - Aspiration pneumonitis (due to delayed gastric emptying time) - Transplacental passage of medications - Uterine atony from inhalation gas - Poorer control of postoperative pain	- Slower - Hypotension (sympathectomy) - Single shot	- Slower - Hypotension but less severe than spinal block (sympathectomy)
Indications	- Emergency Cesarean delivery - Alteration of consciousness (inability to cooperate)	- Most Cesarean deliveries - Absence of neurological manifestations of increased intracranial pressure - Absence of thrombocytopenia or coagulopathy	- Most Cesarean deliveries - Absence of neurological manifestations of increased intracranial pressure - Absence of thrombocytopenia or coagulopathy
Protocols	- Pre-medication: histamine H2-receptor antagonists, 0.3 molar sodium citrate, metoclopramide - Rapid sequence induction with cricoid pressure: thiopental 4 to 5 mg/kg) or propofol (2 to 2.5 mg/kg) succinylcholine (1 to 1.5 mg/kg) - Maintenance: 50% to 70% nitrous oxide followed by volatile anesthetic agent (<1 minimum alveolar concentration; MAC), and non-depolarizing muscle relaxant - Postoperative: midazolam (5 mg), morphine (10 mg)	- Quincke spinal needle number 26 to 27 or Whitacre needle no 25 at L3 to 4 - 0.5% heavy Marcaine (2 mL), morphine 0.2 mg, (dose vary from 7.5 to 10 mg, depending on the patient's height)	- Touhy needle at L3 to 4 - 2% lidocaine (15 to 20 mL by titration technique to effect - 0.0625% Marcaine + 0.02 mg/ml of morphine via epidural for post-operative pain control

L=lumbar level

and interquartile range. The Pearson's chi-square test and Fisher's exact test were used to compare data between the groups. PASW Statistics, version 18.0 (SPSS Inc., Chicago, IL, USA) was used for analyzing data. A p-value of less than 0.05 was considered statistically significant.

Results

There were 113,914 deliveries between January 2005 and December 2017. During this 13-year period, 46 women with O14 and O15 codes (ICD-10) were identified. After a manual review of their EMRs, eclampsia was confirmed in 45 of 46 cases. The clinical details of these women diagnosed with eclampsia are shown in Table 3. It was important to note that only five of 45 (11.1%) were diagnosed with pre-eclampsia before the development of seizures. The systolic blood pressures (SBP) and diastolic blood pressures (DBP) four hours prior to the seizures were 153.9±28.5 and 92.7±19.2 mmHg, respectively (n=20). Only four (8.9%) women with eclampsia had documented prior risk factors. Twenty-five of 45 (55.6%) women reported warning signs such as headache, visual disturbances, nausea, vomiting, and epigastric pain or dyspepsia one week prior to development of eclampsia.

Most eclampsia (29 of 45; 64.4%) occurred prior to onset of labor. Intravenous $MgSO_4$ was used in 30 of 45 (66.7%) women with eclampsia. Combinations with diazepam or thiopental were administered by anesthesiologists for women who seized during Cesarean section or in the ICU after delivery. Ten (22.2%) women with eclampsia in the present study cohort had vaginal delivery and the pain was controlled with intravenous analgesia such as 50 mg of pethidine, of which one out of ten delivered by forceps extraction with an addition of pudendal nerve block. Eclampsia developed prior to onset of labor in two of ten women with eclampsia that delivered vaginally.

Cesarean section was the mode of delivery in 35 (77.8%) women with eclampsia in the present study cohort, of which 17 (48.6%), 17 (48.6%), and one (2.8%) had GA, RA, and combined GA+RA, respectively. The management details are shown in

Table 3. Characteristics of patients with eclampsia (n=45)

Variables	Values; n (%)
Characteristics	
Age (years); mean±SD	24.4±8.5
BMI (kg/m^2);mean±SD	27.1±4.9
Primigravidas	32 (71.1)
Gestational age at delivery (weeks); mean±SD	35.4±3.0
Diagnosis of severe preeclampsia before eclampsia	5 (11.1)
SBP within 4 hours before seizures (mmHg) (n=20); mean±SD	153.9±28.5
DBP within 4 hours before seizures (mmHg) (n=20); mean±SD	92.7±19.2
Prior risks	
Chronic hypertension	2 (4.4)
Gestational hypertension	1 (2.2)
History of preeclampsia in previous pregnancy	1 (2.2)
Symptoms before developing eclampsia	
Preceding symptoms <1 week before seizure	25 (55.6)
Headache	19 (42.2)
Visual disturbance	8 (17.8)
Vomiting	7 (15.6)
Nausea	6 (13.3)
Epigastric pain or dyspepsia	6 (13.3)
Dyspnea	1 (2.2)
Episodes of seizures; median (minimum, maximum)	1 (1, 6)
Period of eclampsia	
Antepartum	29 (64.4)
Intrapartum	8 (17.8)
Postpartum	8 (17.8)

SD=standard deviation; BMI=body mass index; SBP=systolic blood pressure; DBP=diastolic blood pressure

Table 4. Management (n=45)

Variables	Values; n (%)
Control of seizures	
$MgSO_4$	30 (66.7)
Diazepam	1 (2.2)
Thiopental	1 (2.2)
$MgSO_4$ + diazepam	11 (24.4)
$MgSO_4$ + thiopental	2 (4.4)
Control of blood pressure	
Hydralazine	25 (55.6)
Nifedipine	10 (22.2)
Labetalol	1 (2.2)
Combination	9 (20)
Modes of delivery	
Vaginal delivery	10 (22.2)
Cesarean section	35 (77.8)
Choices of anesthesia	
General anesthesia	17 (48.6)
Spinal anesthesia	15 (42.9)
Epidural anesthesia	2 (5.7)
Combined general & spinal anesthesia	1 (2.8)

$MgSO_4$=magnesium sulfate

Table 4. The indications for GA were alterations of consciousness after seizures leading to an inability to cooperate, thrombocytopenia of less than 100,000/mL, non-reassuring fetal heart rate pattern, pulmonary edema, and maternal achondroplasia. Some of these patients were already intubated before transferring to the operating theater because of recurrent seizures, altered level of consciousness, respiratory difficulties, and post-seizure cardiac arrhythmia. In addition, eight women who received spinal anesthesia (53%) experienced a larger than 20% drop of SBP from baseline for more than five minutes, which required resuscitation with low-dose vasopressors. There was no profound hypotension that resulted in neonatal depression as evidenced by low Apgar scores in the present study cohort. Postoperatively, 15 women (33.3%) with eclampsia required admission to ICU for their respiratory or neurological concerns. Out of these, three women with delivery-related complications survived without long-term morbidities. HELLP, a syndrome characterized by hemolysis, elevated liver enzymes, and low platelet count was found in nine of 45 (20%) women with eclampsia. There was one maternal death. The preoperative status of this patient was diagnosed eclampsia with partial HELLP syndrome and elevated aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase (ALP) with pulmonary edema. The patient died at day 10 after delivery due to multiple organ failure that included liver failure, renal failure, and disseminated intravascular coagulation (DIC).

Twenty of 45 (44.4%) women with eclampsia delivered at less than 37 weeks' gestation. The authors recorded three of 45 (6.7%) neonatal deaths attributable to pre-eclampsia or eclampsia, including iatrogenic prematurity from the clinician's decision to initiated preterm delivery. The maternal and neonatal outcomes are shown in Table 5. Correlation between major perinatal outcomes and the choice of anesthesia are shown in Table 6. Patients who underwent GA had a significantly higher rate of ICU admission postoperatively ($p<0.001$). There was no case of neonatal depression as demonstrated by the 5-minute Apgar score lower than 7 after Caesarean delivery in either the GA or RA group.

Table 5. Maternal and neonatal outcomes (n=45)

Variables	Values; n (%)
Post-delivery course	
High dependency obstetric ward	30 (66.7)
Intensive care unit	15 (33.3)
Delivery-related complications	
Postpartum hemorrhage	1 (2.2)
Uterine rupture	1 (2.2)
Cervical tear	1 (2.2)
Preeclampsia-eclampsia related complications	
HELLP syndrome	9 (20.0)
Pulmonary edema	5 (11.1)
Acute renal failure	5 (11.1)
Reintubation	1 (2.2)
Death	1 (2.2)
Birth weight (g); mean±SD	2,361±701.2
Apgar scores	
1-minute; mean±SD	6.4±2.8
5-minute; mean±SD	8.0±3.0
5-minute Apgar score <7	3 (6.7)
Neonatal complications	
Premature birth (<37 weeks)	20 (44.4)
Small for gestational age	13 (28.9)
Neonatal death	3 (6.7)
Hypoglycemia	3 (6.7)
Neonatal ventilator support	2 (4.4)
NICU admission	5 (11.1)

SD=standard deviation; NICU=neonatal intensive care unit

Table 6. Maternal and neonatal characteristics according to choice of anesthesia for cesarean delivery in eclampsia (n=34), after exclusion of a case of combined general anesthesia and regional anesthesia

	GA (n=17); n (%)	RA (n=17); n (%)	p-value
Maternal			
Gestational age <37 weeks	11 (64.7)	11 (64.7)	1
Platelet count <100,000/mm^3	7 (100)	0 (0.0)	<0.001*
Seizure >1 time	9 (52.9)	11 (64.7)	0.52
Antepartum eclampsia	13 (76.5)	14 (82.4)	0.83
Admission to ICU	12 (70.6)	2 (11.8)	<0.001*
Neonatal			
Birth weight <2,500 g	10 (58.8)	12 (70.6)	0.69
5-minute Apgar score <7	0 (0.0)	0 (0.0)	1

GA=general anesthesia; RA=regional anesthesia; ICU=intensive care unit

Discussion

The incidence of eclampsia from the present study was not reported because the population in the present cohort was referral biased. Most eclampsia cases occurred without prior risks, warning signs, or a critically high blood pressure. The present study high Cesarean delivery rate of 77.8% in women with eclampsia was similar to the previous reports, therefore, anesthetic techniques play an important role in optimizing perinatal outcomes[18,19]. The choice of a GA was biased for women with more serious clinical indicators, such as a platelet count lower than 100,000/mL in HELLP syndrome. The higher ICU admission rate in women that underwent GA may be attributable to their pre-existing systematic organ dysfunction, rather than the consequences of the GA itself. There was no difference between GA and RA in terms of seizure control. The effects of GA and RA in babies who were born from women with eclampsia could not be determined due to an absence of neonatal depression after Caesarean delivery in the present cohort. One maternal mortality and three neonatal deaths were attributed to eclampsia and not from the choice of anesthesia.

The present study findings confirmed that pre-eclampsia or eclampsia is indeed a systemic disease, and blood pressure is not a sole predictor of seizures[20]. The reported incidence of eclampsia that occurred prior to the onset of labor or antepartum eclampsia, ranged from 30% to 74%. This broad variation suggests an inconsistency in the diagnostic criteria and definition of eclampsia[21]. Maternal deaths directly attributed to pre-eclampsia or eclampsia virtually do not exist in developed nation[19]. This is partly due to the rise of clinician-initiated preterm delivery at an earlier gestational age, which comes at a cost of neonatal death from prematurity[22].

Both GA and RA pose higher risks for women with eclampsia and her newborn baby. Due to a scarcity of scientific evidence regarding suitable anesthesia in eclampsia, choices are usually individualized to the patient's condition[23]. Altered consciousness after eclamptic seizures have been reported as the most common (75%) indication for GA in a Cesarean delivery[19]. The authors also preferred GA to RA if there was thrombocytopenia to avoid the risk of procedure-related epidural hematoma[24]. An RA may have been safe in women with eclampsia when the platelet count was over 80,000/mL, especially for those at a higher risk of GA-related complications[25,26]. However, the authors have been conservative and adhering to platelet counts greater than 100,000/mL to offer RA because some women with eclampsia may also have had subclinical

consumptive coagulopathy. Maternal hypotension is more significant in RA compared to GA, but this drop in blood pressure does not affect Apgar scores or cord gas findings[27].

The limitation of the present study is the incidence of eclampsia in the authors' institution has been decreased after the implementation of the Institutional Guidelines for Diagnosis and Management of Pre-eclampsia-eclampsia. The number of sample size among groups was low.

Conclusion

Eclampsia remains a cause of serious perinatal morbidities. A prospective study on eclampsia is difficult to conduct because of the rarity of eclampsia due to the availability of

pre-eclampsia prediction and prevention, protocol-based management in suspicious cases, and liberal use of $MgSO_4$ to prevent seizure[28-30]. With proper patient selection and individualization, it is reasonable to assume that both GA and RA are equally safe for women with eclampsia.

What is already known on this topic?

General anesthesia increases maternal risk of cerebral hemorrhage from aggravated hypertension and thrombocytopenia in women with eclampsia. Regional anesthesia increases risk of epidural hematoma in the mother and risk of neonatal depression from profound hypotension. Published evidence for optimal choice of anesthesia for eclampsia is limited.

What this study adds?

With proper patient selection and individualization, either general or regional anesthesia is safe in women with eclampsia.

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Conflicts of interest

The authors declare no conflict of interest.

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