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Optimizing Delivery Strategies in Eclampsia: A Comprehensive Review on Seizure Management and Birth Methods

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Eclampsia seizure is an always serious and potentially fatal obstetric condition. Safe delivery in women with pregnancies complicated by eclampsia seizures is still one of the greatest challenges in perinatal medicine. Pregnancy should be terminated (childbirth) in the safest and least traumatic way possible. Attempting vaginal delivery can take place only exceptionally, in the event of possibly quick completion of childbirth with a stable state of the mother and the fetus. However, immediate labor via cesarean section is most often recommended. It is essential to maintain left lateral patient positioning during cesarean section. Regional anesthesia can be used only in conscious patients who are free from coagulopathy and from HELLP (hemolysis, elevated liver enzymes, and low platelet count) syndrome to decrease the risk of aspiration and failed intubation attempts in preeclamptic or eclamptic women.

For sudden, unexpected interventions, when a patient arrives at the hospital with an eclampsia seizure without lab results, general anesthesia can be the best option and should be performed by an experienced medical team of anesthesiologists, ready to perform difficult intubation.

Magnesium sulfate is the drug that should be used first to stop eclamptic convulsions and prevent their recurrence. Intravenous antihypertensive drugs can stabilize elevated blood pressure (BP), preventing multiorgan failure and recurrent eclampsia seizure, and thus the prevention of maternal death.

This article aims to review the management of seizures during pregnancy in women with eclampsia to ensure safe delivery.

Keywords: Delivery, Obstetric • Emergency Medical Services • Preeclampsia Eclampsia 2 • Pregnancy Complications

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Background

Cerebrovascular events associated with hypertension in pregnancy and preeclampsia are the leading cause of mortality in pregnant and delivering women [1-8]. Pregnancy complicated by preeclampsia is also associated with a 4-fold increased risk of stroke in this group of women [1-8]. Eclamptic seizure and its complications are the leading causes of maternal death in pregnancies complicated by hypertension or preeclampsia with severe features [4,5,7].

Termination of pregnancy (labor) is the first necessary stage of causal treatment of preeclampsia and eclampsia [4]. Safe delivery in women with eclampsia continues to be a challenge.

This article aims to review the management of seizures during pregnancy in women with preeclampsia to ensure safe delivery.

Labor Management – Mode of Delivery

There is no causal treatment for preeclampsia and eclampsia other than childbirth [4,7,9]. Pregnancy should be terminated in the safest and least traumatic way possible. Due to the threats to life and health of the mother and fetus in all women suffering from eclampsia independently of pregnancy advancement, the immediate termination of pregnancy via cesarean section is recommended after stabilizing the patient's clinical condition. The best option is to perform a cesarean section without peritonization using the Misgav-Ladach method with the Douglas' drainage pouch (the peritoneum should not be closed) [10].

In this group of women, attempting natural vaginal delivery can take place only exceptionally, in the event of a possibly quick completion of childbirth with a stable state of the mother and the fetus [11-13]. The dynamics of this condition and the increased risk of a patient's death as a result of eclampsia must be considered. In this regard, in the event of eclampsia, immediately ending the pregnancy by urgent cesarean section is the preferable method of childbirth. The occurrence of an eclamptic seizure attack outside of the hospital is a significant additional risk of complications [3-5,7,11-13].

Bartal and Sibai [13] admittedly allow for the possibility of continuing vaginal delivery and even the possibility of labor induction or acceleration in patients after an eclampsia attack, as long as they are conscious, stable, oriented in place and time, with confirmed fetal well-being, and have their cervix ready for labor (favorable cervix – Bishop score is 6 or greater), and when circumstances indicate the end of labor in the next few hours [13,14]. However, in pregnant women without contractions, it is recommended to perform urgent cesarean section after stabilizing the clinical condition of the patient [13,14]. During cesarean section, the operating table should be slightly tilted by 15°, which allows the patient to be placed on the left lateral side to reduce compression on the inferior vena cava [15].

In patients before the 32nd week of pregnancy, especially when accompanied by intrauterine fetal growth restriction (FGR) and in patients with HELLP syndrome, cesarean section is a method of choice because of the severe unpredictable consequences of the vaginal delivery for both the mother and fetus [13,14]. It must be emphasized that cesarean section in this group of women is always a high-risk treatment procedure [13,14,16-18]. It is essential to perform basic tests such as morphology and thrombocyte level, evaluation of coagulation system, and kidney and liver function tests before surgery (cesarean section), and a crossmatch of blood for possible transfusion is also needed [13,14,16-18].

In one-third of patients with eclampsia, HELLP syndrome will develop. In preparation for surgery, thrombocyte concentrate transfusion may be needed [11-13,16]. Unfortunately, it is not always possible due to lack of time while tests are performed during a cesarean section. This occurs in situations when an unconscious patient with an eclampsia seizure arrives at the hospital or is in the state of eclampsia, often with fetal heart rate abnormalities, with fetal asphyxia posing a threat. In this case, cesarean section is necessary for rescue for the mother and infant [11-13,16].

Many clinicians claim that non-closure of the peritoneum is reasonable (Misgav-Ladach cesarean section is the most commonly performed) and in the event of HELLP syndrome or other coagulation disorders along with thrombocytopenia, leaving the drain in the abdominal cavity in the pouch of Douglas, under the fascia and optionally in subcutaneous tissue [11-13,16-18].

The Choice of Anesthesia

The next point is the choice of anesthesia for a cesarean section. Any type of anesthesia carries a certain risk [18-19].

The decision about general anesthesia is faster and safer for intubated patients. General anesthesia carries the risk of intubation failures and further complications. On the other hand, regional, epidural, or spinal anesthesia contributes to a decrease in blood pressure, which seems beneficial for this group of patients with pregnancies complicated by preeclampsia or hypertension [18-23]. Taking into account the difficulties associated with intubation due to throat laryngeal edema, aggravated in pregnancies complicated by preeclampsia, and thus increased risk of complications in the form of unsuccessful intubation and risk of increase in blood pressure and intracranial

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pressure during intubation, as well as the risk of aspiration syndrome, there are many arguments in favor of regional anesthesia as a preferable option for cesarean section [13,16,19,20]. However, regional anesthesia should be considered only in conscious patients with accurate lab results showing normal coagulation system and adequate levels of platelets. For sudden, unexpected interventions, when a patient arrives at the hospital with an eclampsia seizure without lab results, general anesthesia can be the best option [14,16,18,19].

International consensus regarding a level of platelets (PLT) higher than 70-80×10^9/L is acceptable for performing regional, epidural, or spinal anesthesia [13,16,19-21].

However, anesthesiologists often do not clearly define the lower limit of platelet level needed for the procedure of regional anesthesia for cesarean section. The literature indicates that a level of platelets ranging from 70 to 100×10^9/L is acceptable for cesarean section to avoid events of epidural hematoma [8,11,12,21]. The risk of epidural hematoma within this group has been assessed at about 0.2% (at levels of PLT 70-100×10^9/L) [13,16,21-23]. Sometimes, even lower levels of platelets, around 50 x 10^9/L in patients displaying primary idiopathic thrombocytopenia, can be acceptable to perform spinal anesthesia, which requires a thinner needle than epidural anesthesia, which carries a higher risk of bleeding [11,22-27].

However, the cause of thrombocytopenia should always be considered because it has significant meaning for the rate and suddenness of the change, and for the dynamic trajectory of platelet fall, due to the dynamics of primary disease development, which is a cause of thrombocytopenia. In pregnant women with immunological thrombocytopenia, a quite stable platelet level may rapidly drop when a patient suffers from HELLP syndrome [13,16]. Furthermore, not only the number of thrombocytes is vital, but also their function. It must be considered that in patients with preeclampsia or HELLP syndrome, the functioning of platelets is often impaired even if their level is normal. In addition, the number of platelets can be reduced even before other clinical symptoms of HELLP syndrome appear (lab phase – preclinical phase of HELLP syndrome) [13,16,21]. Therefore, it is always important to approach each patient individually and perform strict clinical observation with lab parameter monitoring in the event of a platelet level lower than 150×10^9/L, especially if previous results were in the normal range.

Because 1/3 of patients with eclampsia develop all symptoms of HELLP syndrome, there is an increased risk of hemorrhage to the subarachnoid space, while regional anesthesia may constitute an additional risk, and it is not recommended in such situations [16,17,26]. Hemorrhage and spinal subarachnoid hematoma in women with HELLP syndrome have been observed [26].

International medical societies recommend regional anesthesia in situations when it is safe to be used to decrease the risk of aspiration and failed intubation attempts in women with preeclampsia [17,18]. The American College of Obstetricians and Gynecologists guidelines confirm that regional anesthesia can be used in severe preeclampsia patients who are free from coagulopathy and HELLP syndrome [19]. In patients with an abnormal fetal heart rate, fetal asphyxia, premature detachment of the placenta, pulmonary edema, HELLP syndrome, or severe thrombocytopenia, general anesthesia is recommended. An individual approach and an experienced medical team of anesthesiologists, ready to perform difficult intubation, are necessary [13,18].

Anesthesia also requires adequate patient monitoring, and it should involve at least standard-level monitoring. Although it is not common, invasive monitoring is sometimes required. Central venous pressure (CVP) monitoring is one of the routine activities performed by anesthesiologists in patients with pulmonary edema, kidney disorders, electrolyte and fluid imbalance, and regional anesthesia [28].

Treatment is Aimed at Stopping the Eclamptic Seizures and Preventing Their Reoccurrence and Complications

Magnesium sulfate ($MgSO_4$) is the best option used in stopping eclamptic convulsions and preventing reoccurrence. Magnesium sulfate infusion with a loading dose of 4-6 g in a drip over 15-20 min and continued at a dose of 1-2 g per hour 24 h after labor, cesarean section, or the last eclamptic seizure protects the patient from reoccurrence [13,22,27,29,30].

Antihypertensive Therapy and Blood Pressure Stabilization

Women with eclampsia must be treated with rapid-acting intravenous drugs to lower high blood pressure. **Table 1** presents drugs used for hypertensive emergencies in patients with eclampsia [31-34].

Postpartum Care and Post-Delivery Management

Postpartum clinical procedure involves intensive medical care treatment, strict supervision, uterine involution, postpartum bleeding, prophylaxis, and fighting infections. Although the delivery of both a baby and placenta constitute the only causal currently known treatment of preeclampsia and eclampsia, it does not eliminate threat to patient life and health, as the

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Table 1. The first choice of antihypertensive drugs with rapid effect by venous infusion is used for hypertensive emergencies in eclamptic women [31-34].

Drug	Mechanism of activity	Dosage	The time when the drug starts its action	Duration of action of the drug	Side effects/ contraindications
Hydralazine	– Reduces the blood vessels' resistance and the vessel's afterload – Relaxes the precapillary arterioles – Dilates blood vessels – Also improves fetal circulation by increasing blood flow in the umbilical vein and leads to increased blood flow in the intervillous spaces, regardless of maternal BP or heart rate [31-34]	2.5-5mg – Repeated administration if necessary every 20 minutes, – Up to a total dose of 20 mg or infusion in a dose of 0.5-10 mg/h [31-34]	5-20 minutes from administration [31-34]	2-6 hours	– Non-threatening short-term side effects in the form of reflex tachycardia and heart pounding, and an increase in cardiac output [31-34] – Rarely chest pain, dizziness, sudden fall in blood pressure, state of fear, face redness, headaches, lower abdominal pain, and fluid retention 31-34 **Caution:** do not use in case of tachycardia above 100 beats per minute
Labetalol	– A non-selective β-blocker and postsynaptic inhibitor of α_1 receptors – Inhibits neuronal uptake of norepinephrine and dilates blood vessels – Leads to a significant drop in peripheral systemic vascular resistance, – Slows the HR and reduces BP while maintaining peripheral circulation at normal levels, also uteroplacental circulation – Without significant impact on maternal cerebral, renal, and coronary circulation – Well tolerated among patients with congestive heart failure and after myocardial infarction – Immediately decreases BP, mostly by vasodilation and a drop in HR – A cardio-selective drug that does not generate endogenous sympathomimetic activity – Recommended for hypertensive patients with tachycardia and myocardial ischemia [31-34]	Starting with a dose of 10-20 mg during the first 2 min and can be repeated with a dose of 20 mg, 40-60 mg, or 80 mg every 20-30 min, or up to a maximum dose of 300mg/day or continuous intravenous injection, in the starting dose of 1-2 mg/min, and subsequent dose of 5-10 mg/h, up to a dose of 300 mg/day [31-34]	After 5 minutes peak activity is reached in 10-20 minutes after its administration [31-34]	6 hours	**Caution:** may occur bradycardia in a mother and fetus [31-34]

mg – milligram; mg/h – milligram per hour; BP – blood pressure; min – minute; h – hour; HR – heart rate.
Created by authors based on literature data [31-34].

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patient has not been completely cured and the threat to life has not passed. At application of adequate therapeutic procedure, in most patients, gradual improvement and remission of symptoms of preeclampsia and HELLP syndrome is achieved in the first week postpartum [13,14].

The need for detailed observation, supervision, and proper choice of treatment must be emphasized because eclampsia may occur postpartum as well as usually within the first 48 h and up to 7 days after delivery [13]. Postpartum, there may be a sudden general worsening of a patient's condition and intensification of preeclampsia symptoms. Furthermore, there is an increased risk of cardiovascular disorder, acute cardiac failure, stroke, and kidney failure or acute kidney injury (AKI), especially in patients with chronic hypertension, a superimposed preeclampsia condition, or kidney injury [35].

In certain groups of postpartum patients, symptoms of preeclampsia can appear for the first time, even without previous irregularities. It is estimated that about 10% of patients had normal blood pressure (BP) earlier. Postpartum eclampsia occurs in 11-44% of cases [14,36] and cannot be neglected. In some patients, late postpartum eclampsia has been observed even later than 7 days after childbirth [8]. Therapy continuation and rigorous supervision for up to 72 h postpartum or longer is advised, depending on the clinical condition of a patient after delivery. Hospital treatment until the 7th day after delivery is indicated, as well as obstetrics control of a patient's state 7-10 days postpartum. Intensive therapy and strict monitoring of a patient's clinical status, along with checking electrolyte and acid-base balance, is required within at least 24-48 h after childbirth.

Particular attention should be paid to the burden on the heart, with a greater amount of circulating blood in the postpartum period resulting from mobilization of fluids from the extracellular extravascular space [37]. This occurs in every woman in the postpartum period, but it is aggravated in patients with edema and severe preeclampsia. Attention should also be paid to fluid balance, intravenous fluid administration, blood pressure, heart workload, kidney and liver function, platelet level, central venous pressure (CVP), and lung auscultation. CVP equal to the pressure in the right atrium is an important parameter of a patient's hemodynamic capacity and circulating blood volume. In this group of patients, there is a higher risk of not only increased blood pressure but also heart failure, kidney failure, DIC (disseminated intravascular coagulation), and pulmonary edema [34,38].

Pulmonary edema is one of the most severe complications. It is observed in 3% of eclamptic patients and its incidence increases in older multiparous women [13,14,19]. It is important to avoid fluid workload and perform an echocardiographic examination when postpartum cardiomyopathy is suspected. These complications are the next most common causes of maternal mortality after a pulmonary embolism [39]. Postpartum patients still require antihypertensive treatment.

Pharmacological blood pressure control prevents hypertension encephalopathy and vascular disorders in the central nervous system (CNS). Blood pressure spikes and an increase in intracranial pressure, or cerebral hemorrhage are associated with increased morbidity and increased risk of death. During the postpartum period in conscious patients, after eclampsia has been overcome, apart from drugs used in the form of intravenous injections, oral antihypertensive treatment can be introduced. Furthermore, postpartum antihypertensive treatment does not have any limitations associated with the presence of a fetus in the uterus [13,14].

Apart from Hydralazine, Labetalol, Ebrantil, and other drugs described earlier in this paper, the introduction of Nifedipine, Methyldopa, and other antihypertensive drugs is possible, depending on the patient's condition [31-34]. The aim of our treatment is not only stabilizing BP, but also the prevention of multiorgan failure and recurrent eclampsia seizure, and thus the prevention of death. A linear correlation has been observed between blood pressure height value (the magnitude of excess pressure), death rate, and future circulation disorder morbidity [14,19,22,31-34]. Furthermore, a higher risk of death due to cardiologic causes and kidney disease has been noted in women who recovered from eclampsia [14]. It must be kept in mind that anticonvulsant therapy must be continued. Magnesium sulfate is most often used to stop and prevent severe eclampsia and preeclampsia. Clinical experience and medical guidelines recommend continuation of magnesium sulfate therapy for at least 24 h up to 48 h after the last eclamptic seizure or delivery [13,14,30,31]. The recommended dose of continued intravenous infusion is usually 1 g/h [30,40].

The main goal of our procedure is to lower blood pressure and stabilize the patient's condition, which requires lowering the elevated blood pressure.

Too-rapid normalization of blood pressure should be avoided, as it carries the risk of a fall in organ blood flow and may lead to brain hypoxia, kidney injury, and cardiac arrest. Systolic BP maintenance at least below 140-150 mmHg, and diastolic blood pressure at level lower than 90-100 mmHg is satisfactory, depending on the patient [14]. With adequate clinical management, quick reduction in antihypertensive drug dosage is often possible. In dealing with patients with preeclampsia or eclampsia not superimposed on other cardiovascular or renal diseases, it is possible to stop the administration of antihypertensive drugs up to 3 months after childbirth, at the latest. However, medical practice shows that these patients

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quite often leave the hospital without further antihypertensive treatment, even patients after eclampsia or eclamptic status [40]. The lack of BP normalization or its spikes is the main cause of treatment failure of eclamptic seizures [11,13,14].

Nifedipine is an especially appreciated drug for its protective effect on the kidneys. It dilates kidney blood vessels contributing to the increase in urine excretion, thereby improving kidney function. Furthermore, in pregnant women with severe hypertension, a beneficial influence on reducing cerebral perfusion pressure has been observed after the administration of even a single Nifedipine oral dose. This is vital due to the high risk of cerebrovascular complications in this group of women. This effect has not been observed after a single dose of Labetalol [28].

Nifedipine is a drug of immediate action, and it provides a rapid decrease in BP without having a serious impact on placental blood flow. This has vital meaning for the well-being of a fetus when administered during pregnancy. It does not disturb fetal heart rate (FHR) in pregnant women [41,42]. However, unexpected sudden hypotensive reactions have been observed. Therefore, this drug has been withdrawn in the United States and Austria. Furthermore, possible interactions with $MgSO_4$ and neuromuscular blockage have caused some controversies [42]. However, most recent research has not confirmed these objections to the use of calcium channel blockers. Magee's research confirms that Nifedipine can be used simultaneously with drugs containing magnesium. The effect of BP reduction is observed within 30 min of administration of Nifedipine [43].

Methyldopa is one of the most commonly-used first-choice antihypertensive drugs for pregnant and breastfeeding women due to its safety profile for mother and newborn, and due to its mechanism of action. However, it can cause depression in patients after childbirth [44]. It works through the stimulation of central receptors and as a blocker of the adrenergic α-2 receptor.

Dosage is 3×250 mg, and the maximum daily dose is 2 g.

Prevention

It has been emphasized that magnesium sulfate should be administered in patients with severe preeclampsia to prevent the occurrence of eclampsia [37]. Magnesium sulfate therapy must also be continued in delivering women or during cesarean section, and a minimum of 24 h after childbirth or during the last eclamptic convulsions [19,27]. Discontinuation of MgSO4 is linked to the risk of eclampsia seizure recurrence. However, magnesium sulfate may predispose the patient to a decrease in muscular strength, weakness of reflexes, respiratory depression, and even pulmonary edema [4,7,13,14,19,27,45].

Edema of the optic nervus disc and an increase in the diameter of the casing sheath of the optic nerve have been observed in severe preeclampsia and eclampsia, and this is correlated with increased cerebral pressure [46-52]. Cerebral edema characteristics may constitute a partial explanation for eclampsia convulsions, posterior reversible encephalopathy syndrome (PRES), and other neurological symptoms [46-52].

Lack of BP normalization or its increases can lead to eclampsia reoccurrence [13,32,37]. However, although hypertension is a characteristic feature of preeclampsia, eclampsia may also occur in patients displaying normal BP values. Furthermore, it seems that there is a slight correlation between BP values and the occurrence of eclampsia attack. Sometimes, a sudden change and worsening of the clinical condition may be difficult to diagnose by objective methods [13,32,37].

Future Directions

This paper aims to discuss problems and ongoing challenges related to clinical management and delivery in eclamptic women targeting lowering maternal and fetal mortality and morbidity related to eclampsia seizures.

Eclampsia is a life-threatening complication of pregnancy and is related to a high risk of maternal and perinatal mortality and morbidity. The incidence of preeclampsia increased over the last decades. Eclampsia is difficult to predict and treat because the pathogenesis of eclampsia seizure is not well understood. Furthermore, eclamptic seizures can also occur in women with normal blood pressure. The only known causal therapy for eclampsia is delivery.

Eclampsia needs to be emergently identified and treated promptly by an interdisciplinary medical team. Communication between all members of the interdisciplinary team is very important.

An intensive care unit is the appropriate place to treat eclamptic women and patients after eclamptic convulsions. However, most often these patients end up in maternity wards.

At the same time, many students and young doctors while specializing sometimes do not have the opportunity to treat eclampsia. Therefore, the entire interdisciplinary medical team must be properly trained to always be prepared for this rare but life-threatening complication that cannot be predicted. Only the engagement of all trained interdisciplinary medical staff (midwives, nurses, physicians, and related professions) can ensure fully professional, immediate, and effective treatment and thus reduce morbidity and mortality in mothers with eclampsia and their infants.

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The close monitoring of hypertensive and preeclamptic pregnant women even without severe features and prophylaxis in the group of pregnancies with high risk of preeclampsia may help to reduce the incidence of eclampsia and its severe complications.

Future research addressing the question of etiopathogenesis of preeclampsia and eclampsia is needed. Understanding the etiology of eclampsia and preeclampsia is of great importance and may in the future lead to inclusion of a causal treatment aimed at the direct cause targeting lowering maternal and fetal mortality and morbidity.

Further research is needed to better understand the mechanisms underlying preeclampsia development and the occurrence of eclamptic seizures to develop effective interventions to improve pregnancy outcomes and quality of life for these women in the future.

Conclusions

Eclampsia seizure is always a serious and potentially fatal obstetric condition. Labor is always beneficial for the mother and is the only currently known causal treatment for preeclampsia and eclampsia. However, safe delivery in women with pregnancies complicated by eclampsia seizures is still one of the greatest challenges in perinatal medicine.

Pregnancy should be terminated in the safest and least traumatic way possible. Attempting vaginal delivery can take place only exceptionally, in the event of possibly quick completion of childbirth with a stable state of the mother and the fetus. However, immediate labor via cesarean section without peritonization with the Douglas' drainage pouch is most often recommended after patient stabilization. Regional anesthesia can be used only in conscious patients who are free from coagulopathy and HELLP. For sudden, unexpected interventions, when a patient arrives at the hospital with an eclampsia seizure without lab results, general anesthesia performed by an experienced medical team of anesthesiologists, ready to perform difficult intubation, can be the best option. Magnesium sulfate is the best drug for stopping eclampsia convulsions and preventing its reoccurrence, and it reduces the risk of maternal death.

Reducing elevated blood pressure is a prerequisite for stopping eclamptic seizures and preventing their reoccurrence. Too-rapid BP normalization should be avoided, as it carries the risk of a fall in organ blood flow and may lead to brain hypoxia, kidney injury, and cardiac arrest. Systolic BP maintenance at least below 140-150 mmHg and diastolic blood pressure at levels lower than 90-100 mmHg is satisfactory. Although hypertension is a characteristic feature of preeclampsia, eclampsia can occur in patients displaying normal BP values.

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