Review Article

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Eclampsia: Preventable Obstetrical Tragedy

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Abstract

Eclampsia is the prominent cause of maternal and perinatal mortality and morbidity. Prevalence of Hypertensive disorders is more in developing countries in contrast to developed countries. Eclampsia, clinical manifestation of severe preeclampsia is discussed with symptomatology. Differential diagnosis of convulsions in pregnancy is reviewed. MgSO4 & Labetalol these two drugs are the backbone in the treatment of eclampsia and ramin boon in desguise. Various protocols for management of Eclampsia are evaluated

Keywords: Maternal mortality; Eclampsia; Convulsions; MGSO4; Edema.

Introduction

Hypertensive disorders are the most common medical complications of pregnancy, with reported incidence between 5% and 10%. [1] The incidence varies from country to country and even region to region of the same country. In contrast to developed countries, prevalence is more in developing countries particularly rural areas contributing significant cause for maternal mortality. Eclampsia, placental abruption, ascitis, hepatic infarction, hepatic rupture, intraabdominal bleeding, pulmonary oedema and acute renal failure are all severe clinical manifestations associated with preeclampsia that can result in maternal death. In the fifth century, Hippocrates noted that headaches, convulsions, and drowsiness were ominous signs associated with pregnancy. In 1619, Varandaeus coined the term *eclampsia* in a treatise on gynaecology.

In this article, we highlight clinical implications of Eclampsia. We focus on monitoring and interventions of this dreaded clinical entity.

Eclampsia, which is considered a complication of severe preeclampsia, is commonly defined as new onset of grand mal seizure activity and/or unexplained coma during pregnancy or postpartum in a woman with signs or symptoms of preeclampsia.

It typically occurs during or after the 20th week of gestation or in the postpartum period. However women in whom eclampsia develops exhibit a wide spectrum of signs ranging from severe hypertension, severe proteinuria and generalized edema to absent or minimal hypertension, no proteinuria and no edema.[2] Most cases of eclampsia present in the third trimester of pregnancy, with about 80% of eclamptic seizures occurring intrapartum or within the first 48 hours following delivery. Rare cases have been reported before 20 weeks' gestation or as late as 23days postpartum[3]. Although the incidence of eclampsia in the developed world has fallen steadily and now less than 1:3000 pregnancies[4],the incidence in some developing countries is as high as 1:1000 pregnancies.[5] Early admission and investigations, use of MgSO4,and timely delivery in women with severe hypertension have been shown to reduce the incidence of eclampsia.[6] The "eclampsia box" recommended by the eclampsia trial collaborative group could be of great

	Douglas & Redman (n=325)(%)	Katz *et al* (n=53)(%)	Chames *et al* (n=89)(%)
Headache	50	64	70
Visual changes	19	32	30
Rt upper quadrant/epigastric pain	19	Not reported	12
At least one	59	Not reported	75

From Sibai BM : Diagnosis, differential diagnosis & management of eclampsia. Obstet Gynecol 105:402,2005.

advantage to under-resourced countries.[7] This includes MgSO4, it's antidote (Calcium gluconate) and necessary paraphernalia to administer the anticonvulsant.

Pathophysiology

The pathophysiology continues to be the subject of extensive investigation and speculation. Several theories and pathologic mechanisms have been implicated as possible etiologic factors but none of these has been proved conclusively. It is not clear whether the pathologic features in eclampsia are a cause or an effect of the convulsions.[2]

Diagnosis

The diagnosis of eclampsia is secure in the presence of generalized oedema, hypertension, proteinuria, and convulsions. However, women in whom eclampsia develops exhibit a wide spectrum of signs ranging from severe hypertension, severe proteinuria, and generalized oedema to absent or minimal hypertension, no proteinuria, and no edema.[2] Symptoms of women with eclampsia

Several clinical symptoms are potentially helpful in establishing the diagnosis of eclampsia. These include headaches, blurred vision, photophobia, epigastric pain. In Author's experience (a series of study of Eclampsia patient, n=201, in 2004-2006, Headache (40%) was the most common warning symptom followed by nausea (25%), epigastric pain (20%).

Hypertension is considered the hallmark for the diagnosis of eclampsia. Hypertension can be severe in 20%-54% of cases or mild in 30-60% of cases. However, in 16% of cases hypertension may be absent. In addition, severe hypertension is more common in patients who develop antepartum eclampsia (58%) and in those who develop eclampsia at 32 weeks gestation or later (71%). Moreover, hypertension is absent in only 10% of women who develop eclampsia at or before 32 weeks of gestation.[3] The diagnosis of eclampsia is usually associated with proteinuria (at least 1+on dipstick). In a series of 399 women with eclampsia, subsequent proteinuria(>3+on diasick) was present in only 48% of the cases whereas proteinuria was absent in 14% of the cases. Several clinical signs and symptoms are potentially helpful in establishing the diagnosis of eclampsia.[3]

Although most cases of postpartum eclampsia occur within the first 48 hours, some cases can develop beyond 48 hours postpartum and have been reported as late as 23 days postpartum. In later cases , an extensive neurological evaluation may be needed to rule out the presence of other cerebral pathology. Cerebral imaging is not necessary for the diagnosis and management of most women with eclampsia. Cerebral

Time of Onset of Eclampsia in Relation to Delivery

	Douglas & Redman (n=383)(%)	Knight (n=214) (%)	Katz (n=53) (%)	Tufnell (n=82) (%)	Matter & Sibai (n=399) (%)	Chmes *et al* (n=89%)
Antepartum	38	96	53	45	53	67*
Intrapartum	18	41	36	12	19	-
Postpartum	4	75	11	26	28	33
<48hr	39		5	24	11	
>48hr	5		6	2	17	7
						26

*Includes antepartum and intrapartum cases

imaging is indicated for patients with focal neurological deficits or prolonged coma. In these patients, haemorrhage and other serious abnormalities requiring specific pharmacological treatment or surgery must be excluded. Cerebral imaging may also be helpful in patients who have an atypical presentation for eclampsia. Advances in MRI as well as cerebral vascular Doppler velocimetry, may aid our understanding regarding the pathogenesis and improving long-term outcome of this condition. In summary, cerebral imaging findings in eclampsia are similar to those found in patients with hypertensive encephalopathy. The classical findings are referred to as posterior reversible encephalopathy syndrome (PRES). Although patients with severe preeclampsia are at greater risk for seizures, 25% of patients have symptoms consistent with mild preeclampsia before the seizures.

Differential Diagnosis

The presenting symptoms, clinical findings and many of the laboratory findings may overlap with a number of medical and surgical conditions. Most common cause of convulsions developing in association with hypertension or proteinuria during pregnancy or immediately postpartum is eclampsia. An effort should be made to identify an accurate diagnosis given that management strategies may differ among these conditions.

Hypertensive encephalopathy, seizuredisorder, hypoglycemia, hyponatremia, TTP, Amniotic fluid embolism, CVAs, Haemorrhage, ruptured aneurism ,Arterial embolism, venous thrombosis, hypoxic ischemic encephalopathy, Agiomas, cerebral malaria, organophosphorus poisoning.

Maternal and perinatal Outcome could be attributed to 3 delays (delay in transport, delay in seeking t/t and delay in diagnosis).In addition, lack of resources and intensive care facilities may be responsible. Eclampsia is associated with a slightly increased risk for maternal death in developed countries (0% to 8%)[2],but the maternal mortality rate may be as high as 14% in developing countries.

Pregnancies complicated by eclampsia are also associated with increased rates of maternal morbidities such as abruption palcentae (7-10%), DIC (7-11%), Pulmonary edema (3-5%), ARF (5-9%), Aspiration pneumonia (2-3%) and cardiopulmonary arrest (2-5%). Rarely ARDS and cerebral haemorrhage may occur.[2] It is important to note that maternal complications are greatest among women who develop antepartum eclampsia, particularly remote from term.

There is high perinatal mortality in eclamptic pregnancies. The reported perinatal death rate is 5.6% - 11.8% high rates of perinatal mortality[2] are attributed to prematurity, abruption placentae and IUGR.

Management of Eclampsia

Eclamptic convulsions are life-threatening emergencies and require the proper treatment to decrease maternal morbidity and mortality. Principles of management include Control of convulsions, control of blood pressure and delivery. Delivery is the only definitive treatment for eclampsia.

Supportive Care

Emergency medical services personnel should secure an intravenous (IV) line with a large-bore catheter, along with cardiac monitoring, oxygen supplimentation and transportion of the patient in the left lateral decubitus position keeping airway petent.

After the seizure has ended, a 16- to 18-gauge IV line should be established for drawing specimens and administering fluids and medications. (Fluid management is critical in patients with eclampsia.) IV fluids should be limited to isotonic solutions to replace urine output plus about 700 mL/d to replace insensible losses.

Pharmacologic Considerations for Control and Prevention of Subsequent Convulsions

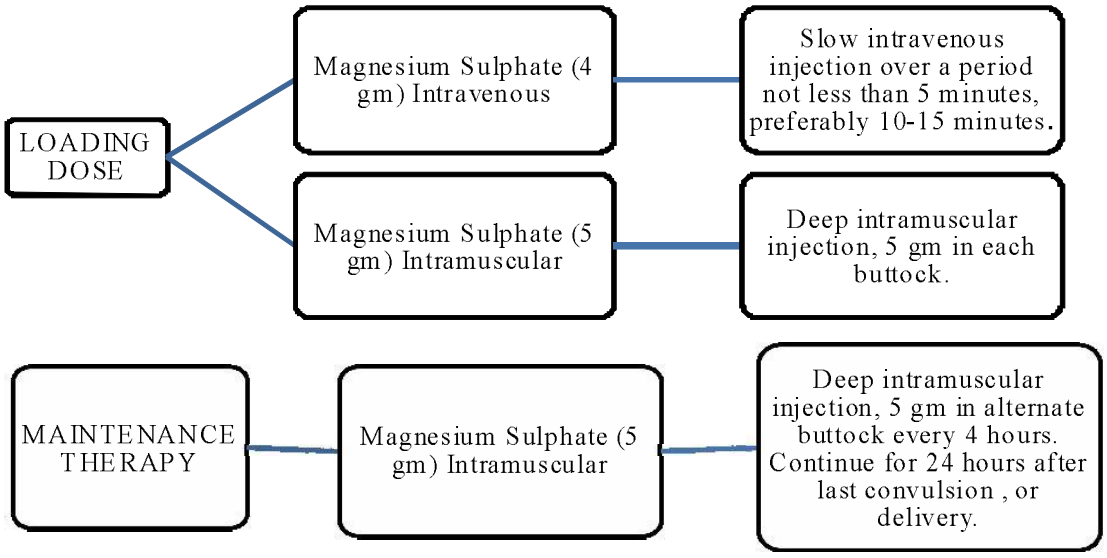
Pharmacotherapy goals are to reduce morbidity, prevent complications, and correct eclampsia. The drug of choice to treat and prevent eclampsia is Magnesium sulphate Familiarity with second-line medications phenytoin and diazepam/lorazepam is required for cases in which magnesium sulphate may be contraindicated (eg, myasthenia gravis) or ineffective.

Treatment Regimens for Magnesium Sulphate (MgSO4)

There were two separate regimens for giving MgSO4 and clinicians at each centre chose which they would use. Both regimens were based on current recommendations and reflected clinical practice in the collaborating centres. An initial intravenous loading dose was followed by 24 hours by either an I/V infusion or regular intramuscular regimen. This

Flow Chart for the Intravenous (I/V) Magnesium Sulphate Regimen

Pritchard & colleagues.



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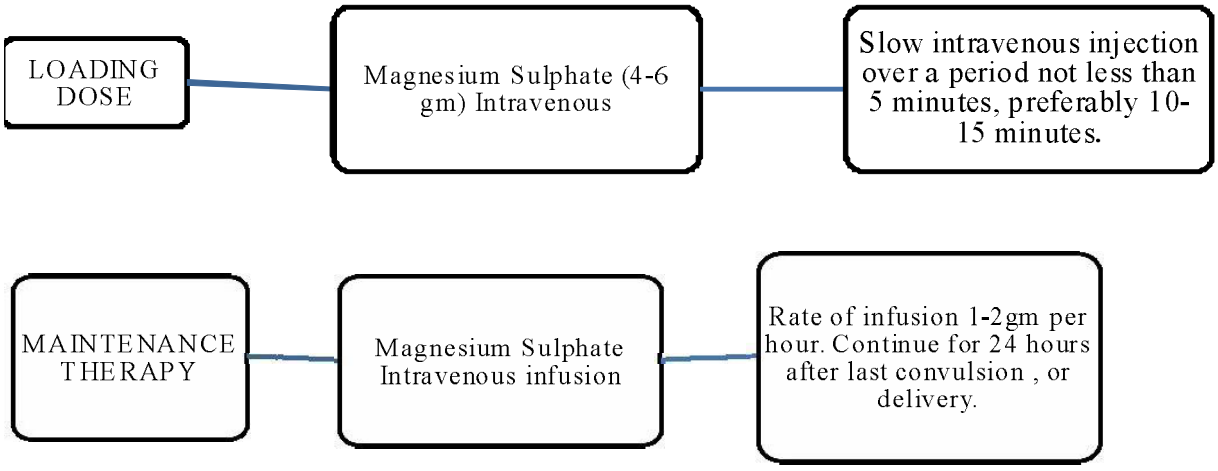

was administered as described by Pritchard & colleagues. A loading dose of 4 gm I/V (usually in 20%solution) over 5 minutes minimum, preferably 10-15 minutes was followed immediately by 5gm in a 50% solution as a deep I/M injection into the upper outer quadrant of each buttock. Maintenance therapy was a further 5 gm I/M every 4 hrs, continued for 24 hours after the last intravenous regimens. The intravenous regimen was as described by Zuspan"s. A loading dose of 4gm I/V was followed by an infusion of 1 gm/hour continued for 24 hours after the last fit. In most centres, the rate of infusion was controlled manually.

Parentral MgSO4 therapy should be continued for at least 24 hours after delivery or for at least 24 hours after the last convulsion.

Recurrent Convulsions

In both the intramuscular and intravenous regimens, if convulsion recur after 30 minutes, a further 2-4 gm was given intravenously over 5 minutes and same dose schedule can be continued. There was no evidence from the Collaborative Trial [8] of any difference between the intramuscular and intravenous regimens in their effects on recurrent convulsions. However intramuscular injections are painful and are complicated by local abscess formation in 0.5% of cases. The intravenous route is therefore preferred. It is rational and sensible for clinicians to adopt the treatment regimens for MgSO4 used in the Collaborative Eclampsia Trial.[8] This has the considerable practical and economic advantage that serum monitoring is not required. Although some authors have advocated 2 gm/h for I/V maintenance therapy, this should not be considered for routine practice until it has been adequately evaluated in comparison to intravenous regimens described here. About 10% of women with eclampsia will have an additional seizure after receiving magnesium sulfate. Another 2 g bolus of magnesium may be given in these cases. For the rare patient who continues to have seizure activity while receiving adequate magnesium therapy, seizures may be treated with sodium amobarbital, 250 mg IV over 3-5 minutes. Alternatively, lorazepam (Ativan) 4 mg IV over 2-5 minutes (may repeat in 5-15 min to maximum of 8 mg in 12 hours) or diazepam (Valium), 5-10 mg IV slowly (may be repeated every 15 min up to 30 mg) can be used per protocol for status epilepticus. However, these drugs can be associated with prolonged neonatal neurologic depression

Magnesium Toxicity and Their Management

The following guidelines were provided for management of the potential complications of MgSO4:

- *Respiratory Arrest:* Stop magnesium therapy and give 1 gm calcium gluconate I/V as antidote for magnesium toxicity along with immediate intubatation and ventilatition. Ventilation should be continued until the resumption of normal spontaneous respiration.
- *Respiratory depression:* Stop magnesium therapy, give 1 gm calcium gluconate I/V along with oxygen mask and maintain airway.
- *Absent Patellar Reflexes:* In case of respiration is normal, further doses of MgSO4 to be withheld/deferred until the reflexes return and if respiration is depressed then manage as above. MgSO4 can be restarted if considered necessary once reflexes have returned but at a reduced dose unless there have been further convulsions.
- *Urine Output-*< 100 *ml in* 4 *h:* If there are no other signs of magnesium toxicity, the next I/M dose of MgSO4 to be reduced to 2.5 gm or the I/V infusion to 0.5 gm/h . Particular attention to be paid to fluid balance and blood loss.

Monitoring during Magnesium Sulphate (MgSO4) Therapy

MgSO4 has no sedative effect, so on recovering from the post ictal phase the

woman should be alert and oriented. However magnesium can depress neuromuscular transmission at the Myoneural Junction, causing muscular paralysis as serum levels increase. The rationale for clinical monitoring is that loss of the patellar reflex (knee jerk) precedes respiratory depression and respiratory arrest. Frequent monitoring of the patellar reflex and respiratory rate are therefore essential if complications of therapy are to be minimised. Also magnesium is cleared by the kidney. So if renal function is impaired, less magnesium will be required. The therapeutic serum level needed to prevent convulsions is generally believed to be between 2 and 4 mmol/L. Loss of patellar reflexes occurs above 5 mmol/L and respiratory depressions at levels above 6 mmol/L. In the Collaborative Trial [8] serum magnesium levels were not measured but data from Sibai *et al.*[9] would suggest that levels were consistently less than 2 mmol/L with this regime. So to measure the serum magnesium was not essential and was not observed in the trial and the protocol for monitoring would be predominantly, clinical and to be based on ensuring that respiration is not depressed, the patellar reflexes are present and renal function is adequate. These can be monitored hourly with recourse to serum levels if there is clinical concern or if further seizures occur.

Summary of Clinical Monitoring during Administration of MgSO4

Only to give the next I/M dose or only to continue the I/V infusion if

- Respiratory rate > 16/min,
- Urine output > 25 ml/h,
- Patellar reflexes are present.

The Collaborative Eclampsia Trial[8] provides compelling evidence that MgSO4 is superior to diazepam and phenytoin for the treatment of eclampsia. It is rational and sensible for clinicians to adopt the treatment regimens for MgSO4 used in the collaborative trial while prejudice may prevent obstetrician from evaluating magnesium but they can no longer justify not using it. It should be feasible to make it clearly and readily available for the care of all women regardless of where they live in countries until now magnesium sulphate has not been routinely used for eclampsia, there should be some regional or national strategy to ensure affordable and regular supplies.

Control of Hypertension: BP should be assessed with the goal of maintaining the systolic BP between 140 and 160 mm of Hg and diastolic BP between 90-105 mm of Hg is reasonable. This can be achieved by using Labetalol or Hydralazine. Diuretics are used only in the setting of pulmonary edema.Care must be taken not to decrease the BP too drastically; an excessive decrease can cause inadequate uteroplacental perfusion and fetal distress.

Maternal Monitoring: Depending on the clinical course, regularly check the patient's neurologic status for signs of increased intracranial pressure or bleeding (eg, funduscopic examination). Keep nothing by

Drug Treatment in Hypertensive Emergencies

Drug	Onset (min)	Peak action (min)	Duration (hr)	Dosage	Mechanism
Hydralazine	10-20	20-40	3-8	5-10mg IV bolus, repeated every 20 min if necessary	Direct dilatation of arterioles
Labetalol	1-2	10	6-16	20 mg IV bolus repeated every 10 min if necessary doubling the dose till 2220 mg	Alpha and beta blocker
Nifedipine	5-10	10-20	4-8	10 mg orally to be repeated after 30 min if necessary	Calcium channel blocker

mouth (including medications) until the patient is medically stabilized or delivered, because she is at risk for aspiration when post ictal and may have recurrent seizures Monitor fluid intake and urine output, maternal respiratory rate, and oxygenation, as indicated, and continuously monitor fetal status. Pulmonary arterial pressure monitoring is rarely indicated but may be helpful in patients who have evidence of pulmonary edema or oliguria/anuria. Once the seizure is controlled and the patient has regained consciousness, the patient's general medical condition should be assessed to identify any other causes for seizures. Induction of labor may be initiated when the patient is stable.

Fetal Monitoring: Fetal heart rate and uterine contractions should be continuously monitored. Fetal bradycardia is common following the eclamptic seizure and has been reported to last from 30 seconds to 9 minutes. The interval from the onset of the seizure to the fall in the fetal heart rate is typically 5 minutes or less. Transitory fetal tachycardia may occur following the bradycardia. Typically, emergent caesarean delivery is not indicated for this post seizure transient bradycardia; it spontaneously resolves.

Delivery (Antepartum or Intrapartum Eclampsia): Delivery is the treatment for eclampsia after the patient has been stabilized. No attempt should be made to deliver the infant either vaginally or by caesarean delivery until the acute phase of the seizure or coma has passed. The mode of delivery should be based on obstetric indications but should be chosen with awareness that vaginal delivery is preferable from a maternal standpoint. Adequate maternal pain relief for labor and delivery is vital and may be provided with either systemic opioids or epidural anaesthesia. In the absence of fetal malpresentation or fetal distress, oxytocin or prostaglandins may be initiated to induce labour. Cesarean delivery may be considered in patients with an unfavourable cervix and a gestational age of 30 weeks or less, as induction under these circumstances may result in a prolonged intrapartum course and is frequently unsuccessful in avoiding caesarean delivery, given the high rate of intrapartum complications. When emergent caesarean delivery is indicated, substantiating the absence of coagulopathy before the procedure is important. Irrespective of gestational age, a prolonged induction with clinically significant worsening of maternal cardiovascular, hematologic, renal, hepatic, and/or neural status is generally an indication for caesarean delivery when the anticipated delivery time is remote.

Surgical Therapy: Cesarean delivery may be necessary for obstetric indications or a deteriorating maternal condition. The patient should be stabilized with respect to seizures, oxygenation, and hemodynamic status before the initiation of cesarean delivery. BP should be controlled and coagulopathies monitored or corrected.

Anesthesia

An anaesthesiology consultation may be obtained. Early evaluation is recommended to assist with cardiopulmonary stabilization and to prepare for a possible operative delivery or endotracheal intubation.

For nonemergency caesarean delivery, epidural or combined techniques of regional anaesthesia are preferred. Regional anaesthesia is contraindicated in the presence of coagulopathy or severe thrombocytopenia (< 50,000 platelets/μL). General anaesthesia in women with eclampsia increases the risk of aspiration, and airway edema may make intubation difficult. It also can produce significant increases in systemic and cerebral pressures during intubation and extubation. The use of spinal anaesthesia requires caution because of the possibility of total sympathetic blockade, resulting in maternal hypotension and uteroplacental insufficiency.

Postpartum Outpatient Monitoring

Follow up 1-2 weeks after delivery to evaluate the patient for BP control and any residual deficits from the eclamptic seizure.

Patients with persistent hypertension past 12 weeks puerperium or neurologic changes may need medical referral. Although the incidence of eclampsia has declined in recent years, mainly due to the improvement of healthcare, serious adverse outcomes still exist five percent of patients with hypertension develop severe preeclampsia, and about 25% of women with eclampsia have hypertension in subsequent pregnancies. About 2% of women with eclampsia develop eclampsia with future pregnancies.[10]

Is Eclampsia Preventable?

Prevention of eclampsia reqires knowledge of it's etiology and pathophysiology and of the methods to predict patients at high risk for development of convulsions. However the pathogenesis of eclampsia is largly unknown. Prevention of eclampsia can be primary by preventing the development of preeclampsia or secondary by employing antihypertensive agents that prevents convulsions in women with established preeclampsia . Prevention can be tertiary by preventing subsequent convulsions in women with established eclampsia..Magnesium sulphate halves the risk of eclampsia, and probably reduces the risk of maternal death. There do not appear to be substantive harmful effects to mother or baby in the short term.[11] Magpie Trial follow up study collaborative Group [12] reported that the reduction in the risk of eclampsia following prophylaxis with magnesium sulphate was not associated with an excess of death or disability for the women after 2 years.

Subsequent Pregnancy Outcome

Women with a history of eclampsia are at increased risk for all forms of preeclampsia in subsequent pregnancies. In general, the rate of preeclampsia in subsequent pregnancies is about 25%,with subsequently higher rates if the onset of eclampsia was in the second trimester. The rate of recurrent eclampsia is 2%.[10]

Conclusion

Eclampsia is a common complication still associated with high level of maternal and perinatal mortality as well as morbidity. Eclampsia is an obstetrical emergency posing significant burden on heath care system. A systemic and well begun programme with a positive thinking will definitely show road to success to accept the challenges. ANC coverage should be strengthened to detect preclampsia, and prevent eclampsia. Management in the hospital should be optimized to prevent recurrent convulsions and complications after admission.

The "Eclampsia box" recommended by Eclampsia trail collaborative group could be of great advantage to under-resourced countries. This includes magnesium sulphate, it's antidote calcium gluconate,and the necessary paraphernalia to administer the anticonvulsant Prompt evaluation and aggressive management of patient with control and prevention of convulsions with MGSO4, control of Hypertension, termination of pregnancy with supportive care will definately reduce mortality and morbidity of this lifethreatening condition.

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