TECHNICAL BRIEF

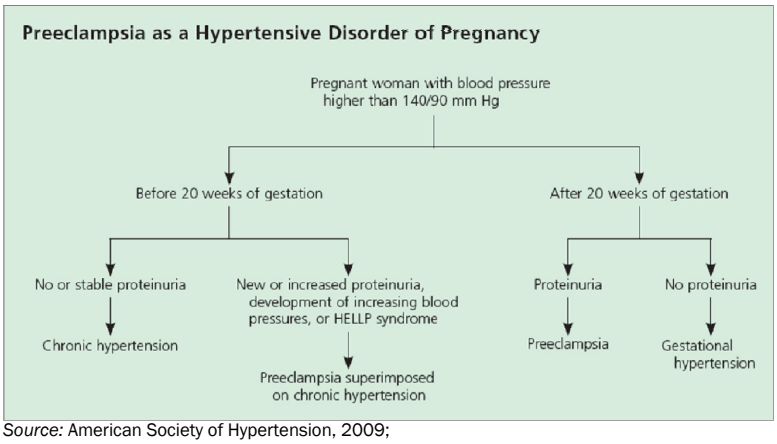
Pre-Eclampsia/Eclampsia: Prevention, Detection and Management

WHAT IS PRE-ECLAMPIA/ECLAMPSIA (PE/E)?

Hypertensive disorders of pregnancy are a unique group of disorders that cause serious morbidity and mortality for both the mother and the baby. While the underlying cause is hypothesized as a poorly-implanted placenta, the clinical symptoms of PE/E typically present after 20 weeks gestation as high blood pressure (BP) and protein in the urine. It may progress from a mild hypertensive disorder to a life-threatening condition (see Table 1), and it is difficult to predict progression. All pregnant women should be monitored for the development of preeclampsia. Certain women with the following characteristics may benefit from additional monitoring:

- A personal or family history of PE/E
- Specific pre-existing medical conditions, such as obesity, chronic hypertension or diabetes
- Age—teen pregnancy and women older than 35 years
- Primigravida
- Related poor outcome of previous pregnancy, including intrauterine growth retardation (IUGR), abruptio placentae, or fetal death
- First pregnancy with a new partner

Figure 1. Diagnosing PE



Source: American Society of Hypertension, 2009; http://www.aafp.org/afp/2004/1215/p2317.html#afp20041215p2317-b5

While these characteristics help providers screen pregnant women, PE remains difficult to prevent or predict. Because severe PE/E is associated with increased risk of adverse outcome for both the mother and the fetus, diagnosing PE and managing it before it progresses to eclampsia is a critical maternal and newborn health strategy. It can also reduce the risk in future pregnancies, as women with a history of eclampsia are at increased risk of eclampsia (1–2%) and PE (22–35%) in subsequent pregnancies.[1] For these reasons, all pregnant women need access to a range of evidence-based prevention, detection and management care.

Table 1. Diagnoses in the Progression to Eclampsia

Probable Diagnosis	Typical Signs and Symptoms
Chronic hypertension	Diastolic BP 90 mm Hg or more <20 weeks of gestation
PE superimposed on chronic hypertension • Women with hypertension and no proteinuria early in pregnancy (<20 weeks' gestation)	In women with hypertension <20 weeks gestation any of the following are seen after 20 weeks: • New-onset or worsening proteinuria, or • Sudden increase in BP in a woman whose hypertension has previously been well controlled
Gestational hypertension • Transient hypertension of pregnancy if PE is not present at the time of delivery and BP returns to normal by 12 weeks postpartum (a retrospective diagnosis)	• Two readings of diastolic BP 90 mm Hg or more but below 110 mm Hg 4 hours apart >20 weeks gestation • No proteinuria

Table 1. Diagnoses in the Progression to Eclampsia	
Probable Diagnosis	**Typical Signs and Symptoms**
Mild PE	• Two readings of diastolic BP 90–110 mm Hg 4 hours apart • Proteinuria up to 2+
Severe PE	Diagnosis of PE (by the above stated criteria) PLUS one or more of the following diagnostic criteria: • Diastolic BP 110 mm Hg or more • Proteinuria 3+ or more • Hyperreflexia • Headache (increasing frequency, unrelieved by regular analgesics) • Blurred vision • Oliguria (passing less than 400mL of urine in 24 hours) • Upper abdominal pain (epigastric or right upper quadrant pain) • Pulmonary edema
Eclampsia	PE with: • Convulsions or • Coma (unconscious)
Source: MCHIP. Prevention and management of pre-eclampsia and eclampsia. Reference Manual for Healthcare Providers. 2011.	

STRATEGIC APPROACHES TO PE PREVENTION

Evidence from both developed and developing countries suggests that deaths associated with hypertensive disorders of pregnancy are the most difficult to prevent.[2] PE/E programming can focus on three strategic approaches to prevention of morbidity and mortality:

- Primary prevention—Avoiding the development of the disease; avoiding pregnancy and conditions favorable to PE development
- Secondary prevention—Detecting the disease early, before clinical symptoms appear
- Tertiary prevention—Treating the disease early in order to prevent progression and complications

These three approaches to prevention can also be thought of as preventing, detecting and managing PE/E. Skilled birth attendants (SBAs) have a critical role to play in these efforts, particularly SBAs in peripheral health care facilities who do the following: provide antenatal care (ANC); counsel women and their families; and screen for PE and can initiate treatment—first intramuscular (IM) dose of magnesium sulfate and the first dose of anti-hypertensive medications—prior to transfer to a comprehensive emergency obstetric and newborn care (CEmONC) facility with capacity for obstetric surgery and management of complications. This technical brief focuses on care that can be delivered by SBAs at home or in a peripheral outpost or referral facility.

Primary Prevention of PE: Calcium Supplementation and Other Interventions

Primary prevention for PE is difficult because its cause is not well understood and associated factors are difficult to influence. Numerous interventions have been studied and reviewed for PE prevention, and Table 2 summarizes the latest evidence on potential interventions for PE primary prevention.

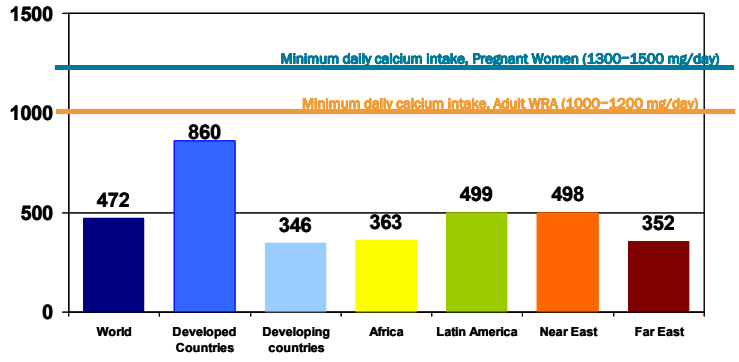
Table 2. Evidence for Primary Prevention Interventions for PE/E		
Intervention	**Pregnancy outcome**	**Recommended?**
Prevention of IUGR	Prevention of IURG theoretically contributes to primary prevention of PE in the next generation	Yes
Family planning	Potential to reduce pregnancies at risk for PE	Yes
Pre-conceptual prevention and/or treatment of obesity	Potential to reduce PE	Yes
Calcium supplementation	• Reduces PE in those at high risk and with low baseline dietary calcium intake • No effect on perinatal outcome	Yes, for those with high risk of gestational hypertension or low dietary calcium intake
Low-dose aspirin	• Reduces PE • Reduces fetal or neonatal deaths	Yes, for populations at increased risk of developing PE
Magnesium or zinc supplementation	No PE reduction	Insufficient evidence to recommend
Fish oil supplementation and other sources of fatty acids	No effect on low- or high-risk populations	Insufficient evidence to recommend
Heparin or low-molecular weight heparin	Reduces PE in women with renal disease and thrombophilia	Insufficient evidence to recommend
Anti-oxidant vitamins (C, E)	Reduced PE in one trial but not in all trials	Insufficient evidence to recommend
Protein or salt restriction	No effect	No
Source: MCHIP. Prevention and management of pre-eclampsia and eclampsia. Reference Manual for Healthcare Providers. 2011.		

Family planning is an effective primary prevention strategy to prevent, delay and space pregnancies, effectively removing PE risk, and treatment of obesity is an effective pre-conception intervention. However, calcium and low-dose aspirin supplementation have the most potential as targeted public health strategies for PE reduction in pregnant women.

Calcium Supplementation

Calcium supplementation shows promise as a large-scale public health intervention to prevent PE among high-risk or calcium-deficient populations. In developing countries, pregnant women do not consume enough calcium. From a WHO systematic review (1991–2004) of dietary calcium intake in pregnant women, calcium intake in Africa and Asia ranged between 200–500 mg/day. Sufficient daily calcium intake is estimated at 1000–1300 mg for non-lactating women of reproductive age.[3]

Figure 2. Levels of Daily Dietary Calcium Intake



Source: Calcium and Prevention of Pre-eclampsia: Summary of Current Evidence, Monitoring, Evaluation and Research Task Force of the PE/E Working Group. 2010.

Based on findings from a WHO randomized controlled trial, pregnant women with low dietary calcium intake who took daily calcium supplements had significantly lower rates of severe gestational hypertension and eclampsia.[4] Most recently, a 2010 Cochrane review looked at the effect of calcium supplementation during pregnancy on hypertensive disorders of pregnancy and related maternal and child outcomes. There were 13 studies of good quality (n=15,730 women). The selection criteria of most of those studies identified pregnant women who were at low risk for PE and who had a low calcium diet. The key findings were that calcium supplementation appears to approximately halve

the risk of PE and to reduce the risk of preterm birth. Specifically, calcium supplements reduced the average risk of high BP and of PE—with the greatest effect in high-risk women and those with low baseline calcium intake. Calcium supplementation did not, however, reduce the risk of severe PE/E or stillbirth.[5] (Please see the annotated bibliography for more detailed information regarding these studies.)

Because there are no adverse effects, calcium supplementation is generally considered to be relatively safe and should be considered in calcium-deficient settings. As a maternal and child survival strategy, maternal calcium supplementation has been identified as having sufficient effect on maternal and birth outcomes to consider it as a public health intervention in low-resource settings, when appropriate.[6] Assuming calcium supplementation has a similar effect on deaths due to hypertensive disorders, universal calcium supplementation could prevent as many as 21,500 maternal deaths annually and reduce disability-adjusted life years (DALYs) by 620,000.[7]

Low-Dose Aspirin

The review of 59 trials, involving 37,560 women, found low doses of aspirin reduced the risk of PE by about a sixth (17%), with a similar lowering in the risk of the baby dying (14%), and a small lowering in the risk of the baby being born too early (8%).[8] Studies to date have shown no significant effect, however, on maternal death, fetal or infant death, or the birth of babies who are small for gestational age.[9] There is no evidence of harm from low-dose aspirin therapy regardless of the woman's risk status,[10] but routine aspirin supplementation is not a recommended prevention strategy for women without risk factors. Although aspirin thins the blood and reduces clotting, low-dose aspirin has not increased risk of hemorrhage (postpartum or antepartum) or infant bleeding. Research suggests that low-dose aspirin needs to be started before 16 weeks of pregnancy to significantly reduce PE.[11]

Secondary Prevention of PE: Early Detection

Secondary prevention strategies focus on early detection of PE—before clinical symptoms become apparent—when other interventions can improve outcomes for the mother and baby. Routine screening of all pregnant women is the only way to detect PE; there are no reliable tests or symptoms for predicting which women will develop PE/E.[12]

Evidence (Table 3) supports two screening tests for detecting PE: measuring BP and protein in urine. WHO guidelines on ANC recommends four ANC visits during a pregnancy, measuring the BP of all women at every visit, and checking for protein in the urine of women found to have elevated BP.[13] Because a woman developing PE rarely has proteinuria before there is a rise in her diastolic BP,[14] WHO ANC guidelines focus on BP history and measurement. Both elevation in blood pressure and the presence of protein in the urine are always pathological in a pregnant woman. Therefore, it is best to screen for both conditions, if possible, at every antenatal client contact, whether in the community or at the facility. Challenges to routine screening include lack of functioning BP apparatus, lack of provider skill in measurement of BP or urine protein, inadequate time spent with woman during ANC visit, cost of proteinuria tests, and logistics.

Table 3. Evidence for Interventions to Detect and Screen for PE

Intervention	Pregnancy outcome	Recommended?
BP screening during ANC	• Screening for elevated BP does not prevent PE • Early diagnosis of PE allows for early and better management, and can prevent progression to severe PE/E, thus reducing adverse maternal and fetal outcomes	**Yes**
Urinary protein screening if diastolic BP greater than 90 mm Hg during ANC	• Screening for urine protein does not prevent PE • Early diagnosis allows for early and better management, and can prevent progression to severe PE/E, thus reducing adverse maternal and fetal outcomes	**Yes**

BP Screening

Due to the physiological changes of pregnancy, hypertension is uncommon in the first half of pregnancy, but occurs in about 10% of pregnancies after 20 weeks. An elevated diastolic BP of 90 mm Hg, when taken two times and four hours apart, can indicate chronic hypertension, PE super-imposed on chronic hypertension, gestational hypertension, mild or severe PE, or eclampsia.

In low-resource settings where proteinuria testing is not routinely available, the clinical decision-making around PE will depend on an accurate BP measurement. In both developed and developing countries, BP is often incorrectly measured and recorded. In addition to a well-calibrated device and a good quality stethoscope, measuring BP in low-resource settings requires a competent and experienced provider. The conventional auscultation technique is often poorly performed, as illustrated by ANC clinic findings in Tanzania, where health workers detected only 4 out of 12 cases of elevated BP among 379 patients. Equally concerning, more than 100 women were not even checked for elevated BP,[15] highlighting missed opportunities for PE screening during ANC. Given the close association between elevated BP at ANC and subsequent diagnosis of PE, careful assessment of BP during ANC is warranted.[16]

URINARY PROTEIN SCREENING

Proteinuria is defined as the presence of 300 mg or more of protein per liter in a clean-catch, midstream specimen of urine.[17] Proteinuria tests are most commonly available in developing countries as urine dipstick or boiling tests. Esbach (24-hour urine proteinuria) and urine protein:creatinine ratio are sometimes used in tertiary care facilities. Although a study in Pakistan found dipstick urinalysis less accurate than the 24-hour urine protein measurement,[18] the simplicity, ease of use, and rapid results make the dipstick test suitable for screening in high volume, low-resource ANC settings. Proper storage and handling of dipstick tests is required for accurate results.

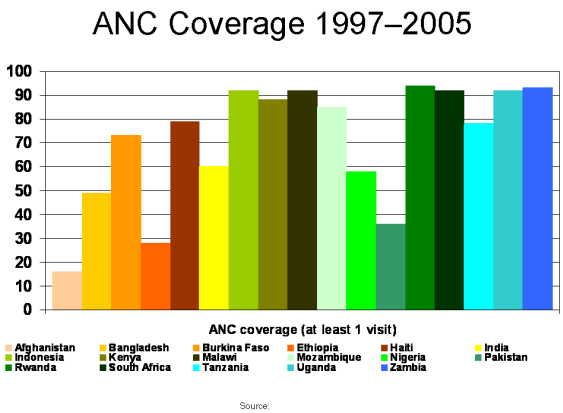
Presence of proteinuria with hypertension gives the diagnosis of PE. Most studies do not demonstrate the degree of proteinuria that correlates with severity of disease. Therefore, the presence of proteinuria—rather than the severity or change in the amount of proteinuria—should be the principle criteria used for management.[19]

ANC

Because PE detection occurs principally during ANC, the quantity and quality of ANC visits is important for secondary prevention to reach all pregnant women. Most women present for ANC in their first trimester, before PE typically begins to develop.[20] Subsequent visits allow opportunities for numerous proven interventions that affect the health of the mother and baby, including opportunities for detection and management of PE.

However, although approximately two-thirds of women in low- and middle-income countries have at least one ANC visit, less than half of women (47%) worldwide receive the recommended four ANC visits (see Figure 3).[21] In some countries, less than one-third of women attend ANC at all, and in Ethiopia, for example, just 12% of women have any ANC.[22] Moreover, rural women are half as likely as urban women to report having four or more ANC visits—the same women who are also less likely to have timely access to life-saving emergency obstetric care should eclampsia develop.

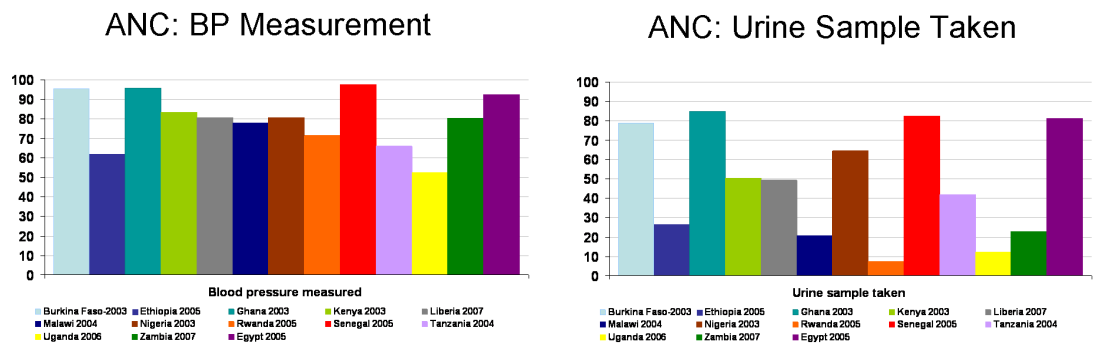
Figure 3. ANC as an Opportunity for PE Detection



Source: Mandel B, Evidence Base for PE/E Strategy, 2009.

The number of visits alone will not save lives, of course, unless high-quality, effective interventions are delivered during those visits. During ANC, more women generally have their BP taken than have their urine tested (see Figure 4). Some evidence suggests that the frequency of screening may not lead to improved care. For example, in a low-resource setting with a high incidence of eclampsia in Tanzania,[23] ANC practice alone was not effective at preventing eclampsia. In that clinic, a screening approach during ANC for detection of elevated BP achieved 95% coverage, and 33% coverage for proteinuria. Among those women, however, less than 50% who developed eclampsia had been referred from ANC clinics, and less than 10% were admitted to the antenatal ward before the onset of eclamptic fits. This suggests that a screening and early detection approach that focuses on only those who attend an ANC clinic would be inadequate.

Figure 4. PE Detection in ANC in Africa



Source: DHS of African Countries (years as noted above)

Several factors may contribute to the poor performance of ANC approaches for detection of PE. These include: insufficient quality of the screening process (accuracy of BP and proteinuria measurement); lack of a functioning system for referral of women with evidence of PE; and substandard treatment approach for those women with PE who are referred. Counseling and patient education are essential—and often undervalued—components of ANC. Because women are frequently asymptomatic when diagnosed with PE, the ability to prevent eclampsia is limited by a woman's and her family's understanding of the underlying cause, warning signs and potential consequences.

Tertiary Prevention of PE: Management

Once severe PE/E is diagnosed, the management focus is primarily through four main evidence-based interventions: anti-convulsant therapy; anti-hypertensive treatment; careful patient monitoring; and timed delivery of the baby. Management of mild PE includes regular measurement of BP and urine and careful monitoring of the woman for signs that the disease may be advancing. No diuretics, anticonvulsants or anti-hypertensives are indicated for mild PE.

In the management of severe PE/E, all SBAs should have the ability and opportunity to provide the first three interventions mentioned above. Whether it is in the home or in a peripheral health care facility, all SBAs should be able to give at least the first dose of anti-hypertensive and anti-convulsive medications prior to transfer to a CEmONC facility for further monitoring, management and, potentially, operative delivery.

It is essential to remember that the only effective treatment for severe PE/E is delivery of the woman. Monitoring of the woman and administration of appropriate medications is a management strategy for preventing further morbidity or mortality while the woman is being delivered, regardless of whether it is a vaginal or cesarean birth.

Table 4. Treatment Interventions for Severe PE/E		
Intervention	**Pregnancy outcome**	**Recommended?**
Magnesium sulfate	• Reduces the risk of eclampsia without any substantive effect on longer-term morbidity and mortality for the women or children	Yes, for severe PE/E *When MgSO4 is not available, diazepam can be used*
Anti-hypertensive drugs	• Improves maternal outcome • Helps reduce maternal complications such as stroke	Yes, if diastolic BP is 110 mm Hg or more
Induction of labor	• Improves maternal and fetal outcome when carried out according to recommendations for severe PE/E	Yes, regardless of gestational age, if severe PE/E. Yes, if mild PE and >37 weeks gestation. If mild PE and <37 weeks gestation, expectant management indicated. Induce labor if severe PE develops.
Source: Prevention and management of pre-eclampsia and eclampsia Reference Manual for Healthcare Providers, MCHIP, 2011.		

Anti-convulsant Therapy: Magnesium Sulfate

Magnesium sulfate is a unique and inexpensive drug that can treat severe PE, and prevent *and* treat eclampsia. In women with severe PE, magnesium sulfate was found to reduce the occurrence of eclampsia by more than 50%[24] and maternal deaths by 46%.[25] It reduces the risk of eclampsia[26] without any substantive effect on longer-term morbidity and mortality for the women or children.[27]

> Implementation of protocols for the use of magnesium sulfate should be a part of every country's maternal mortality reduction efforts.

WHO has identified magnesium sulfate as the most effective and low-cost medication for treatment of eclampsia. It is more effective in reducing the recurrence of convulsions and seizures than diazepam, phenytoin or other drugs.[28] In addition, it is safer and can be more easily used by lower level providers due to its wide therapeutic range.

Despite the evidence and low cost, magnesium sulfate is not widely available in many countries. Less effective and higher-risk drugs (such as diazepam and phenytoin) are still commonly used in most developing countries. While the standard Pritchard regime for administration of magnesium sulfate can be cumbersome and challenging to use, other anti-convulsant regimens have been inadequately studied to date. This regimen combines a loading dose given by both the IM and intravenous (IV) route, followed by IV maintenance therapy for 24 hours following the delivery. During maintenance, monitoring is required to ensure that the patient does not show evidence of magnesium excess—reduced respiratory rate, decreased urine output, or absent Patellar reflexes. Respiratory arrest, although extremely rare, is possible. It is easily treated, however, with calcium gluconate, which antagonizes the effects of magnesium sulfate. No suitable and widely available antidote to diazepam or phenytoin overdose exists.

Interest remains in alternative regimes that could reduce the cost and time (without the 24 hours of maintenance), and simplify the level of care (without IV administration and toxicity risk). A single IM loading dose of magnesium sulfate alone, if given without delay, may be sufficient for the majority of patients.[29] For women with severe PE/E being cared for in more peripheral health facilities, the loading dose given before referral and transport to a hospital has been shown to reduce the number of convulsions, control convulsions (94% compared to 74% in the control), shorten time to full consciousness, and reduce maternal mortality and stillbirths.[30] Two trials (in Pakistan and Bangladesh) compared loading dose alone with the standard Pritchard regime and found equivalent effectiveness between groups in recurrence of convulsions and stillbirth.[31]

According to the latest Cochrane review in 2010, there is still insufficient evidence regarding these shortened regimens to recommend them for wide adoption.[32] The loading dose of magnesium sulfate before transfer to a CEmONC facility is the recommended standard of care for severe PE/E in order to stabilize the woman and improve outcomes for both her and her baby.

Therefore, it is recommended that all women diagnosed with severe PE/E be given the standard Pritchard regime of magnesium sulfate. Moreover, all facilities that use magnesium sulfate should have an ampoule of calcium glutonate, the antidote to magnesium sulfate, available in case of respiratory arrest. If a woman stops breathing, calcium gluconate 1g (10mL of 10% solution) is given by IV slowly over 5–10 minutes.[33]

In collaboration with colleagues in three clinical centers in India, investigators are conducting a pilot study to examine the introduction of a simple, inexpensive, automated flow controlled pump, the Springfusor®, for the continuous infusion of magnesium sulfate. It is hoped that this will be a means of delivering magnesium sulfate that is accurate, easy to use, cost-effective, and with less demand on staff time.[34]

Anti-hypertensive Treatment

A woman with severe PE/E should be monitored closely and her BP measured at least hourly. If the diastolic BP is found to be 110 mm Hg or more, the woman should receive an anti-hypertensive to reduce the BP to prevent cerebral hemorrhage or stroke. The anti-hypertensive is slowly given to reduce the BP and maintain the diastolic BP between 90–100 mm Hg, thus reducing maternal risk without harming the fetus. BP is reduced incrementally in order to avoid an abrupt fall in BP, which can lead to maternal cerebral hypoperfusion and stroke.

While definitive choice of anti-hypertensive drugs remains unclear, labetalol, hydralazine and nifedipine are currently widely recommended. Labetalol is an adrenergic receptor blocking agent, a class of drugs generally considered safe in pregnancy, and the dose of which can be easy titrated to reach the desired effect. The safety record of labetalol in pregnancy, however, is not as well established as methyldopa, although the effect of methyldopa is not as great. Although experience with calcium antagonists (nifedipine) is limited, no increase in major teratogenicity from first-trimester drug exposures has been found. By subgroup analysis, beta-blockers could be less effective than calcium channel blockers.[35]

Once severe PE or eclampsia is diagnosed, SBAs should give at least the first dose of anti-hypertensive medications prior to transfer to a higher-level facility with CEmONC capacity.

Timed Delivery

Even when PE is mild and stable, induction of labor is associated with improved maternal outcome and should be advised for women beyond 37 weeks gestation.[36] For pregnancies prior to 37 weeks, expectant management with careful monitoring is appropriate. In a study from South Africa, a strategy of expectant management for severe PE diagnosed before 37 weeks resulted in the ability to extend pregnancies by a mean of 11 days gestation with improved perinatal and neonatal survival rates.[37] If it is determined that the woman should be delivered prior to 37 weeks gestation, the mother should be given antenatal corticosteroids in an effort to reduce the risk of neonatal respiratory distress syndrome and newborn mortality. Treatment consists of 2 doses of betamethasone 12 mg IM, the first dose given immediately and the second dose given 24 hours later.

For the woman with severe PE or eclampsia, WHO recommends that delivery take place as soon as her condition is stabilized. Substantially delaying delivery in order to increase fetal maturity will risk the lives of both the woman and her baby. Delivery should occur regardless of the gestational age. In severe pre-eclampsia, delivery should occur within 24 hours of the onset of symptoms. In eclampsia, delivery should occur within 12 hours of the onset of convulsions. If the cervix is favorable (soft, thin, beginning to dilate), labor may be induced. However, if vaginal delivery is not anticipated within 12 hours (for eclampsia) or 24 hours (for severe PE) or if the fetal heart rate becomes abnormal, the woman should be delivered by caesarean section.[38]

Monitoring

Vigilant monitoring of a woman with severe PE/E is essential to a healthy outcome for her and her baby. Vital signs and fetal heart rate should be measured hourly and recorded on the partograph. Strict fluid balance of input (IV or other) and urine output should be maintained. Patellar reflexes should be tested hourly and lungs auscultated hourly for presence of rales/pulmonary edema. If possible, clotting should be assessed with a bedside clotting test, as coagulopathy is common in severe PE/E. If a woman is in labor and 4 cm or more dilated, she should also be monitored using a partograph. This instrument guides observation and recording of the condition of mother and baby and the progress of labor, and assists with decision making regarding labor induction. In addition, before repeat administration of magnesium sulfate, respiratory rate (at least 16 per minute), patellar reflexes (present), and urinary output (at least 30 mL per hour over 4 hours), must be assessed.

Foremost in the management of a woman with severe PE/E, the woman should never be left alone. A convulsion followed by aspiration of vomit may cause death of the woman and fetus. In addition to the management of convulsions or unconsciousness in a woman with eclampsia, additional care needs to include: 1) starting an IV or normal saline or Ringer's lactate; 2) inserting a bladder catheter to monitor urine output and proteinuria; 3) providing comfort measures; and 4) continually communicating with the woman and her family concerning her condition and what to expect.[39]

EXPANDED COMMUNITY ROLE

While this paper has focused on the clinical aspects of PE/E, the realization is growing that the incidence of PE/E in a population will not be reduced without community involvement. In order to reach women, especially those who are not seen by an SBA during pregnancy or labor, the role of the community health worker (CHW) must be expanded to include appropriate interventions for the prevention and early detection of PE/E in the community. The CHW could be engaged in efforts to prevent PE through antenatal calcium supplementation. CHWs are already providing community-based education to pregnant women and teaching these women and the community about the danger signs of PE/E, including where and how to seek immediate help. Efforts are also being made to develop simple BP and urine protein detection devices that can be used for screening at the household level. And similar to the Springfusor® automated pump, attempts are being made to develop a safe device to administer a premeasured dose of magnesium sulfate by providers who have little or no experience in parenteral injection.

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