

Evaluation and management of severe preeclampsia before 34 weeks' gestation



Publications Committee, Society for Maternal-Fetal Medicine, with the assistance of Baha M. Sibai, MD

Introduction

Preeclampsia is a multisystem disorder that can manifest clinically with hypertension and proteinuria with or without accompanying symptoms, abnormal maternal laboratory test results, intrauterine growth restriction, or reduced amniotic fluid volume.¹ The incidence of severe preeclampsia ranges from 0.6-1.2% of pregnancies in Western countries.²⁻⁵ Preeclampsia <37 weeks' and severe preeclampsia <34 weeks' gestation complicates 0.6-1.5% and 0.3% of pregnancies, respectively.^{3,6} The likelihood of severe and preterm preeclampsia is substantially increased in women with a history of preeclampsia, and in those with diabetes mellitus, chronic hypertension, or a multifetal gestation.^{1,3,7-10} Published reports use differing criteria for the diagnoses of preeclampsia, severe and superimposed preeclampsia, and HELLP (hemolysis, elevated liver enzymes, low platelets) syndrome. Commonly used definitions are presented in the Table.¹¹⁻¹⁴ For women with preexisting hypertension or proteinuria, the diagnosis of severe preeclampsia can be more difficult, but new-onset severe hypertension or proteinuria, or development of other clinical or laboratory findings of severe preeclampsia are suggestive of preeclampsia in this setting.

Severe preeclampsia occurring preterm can result in both acute^{1,2,4,7-10} and long-

OBJECTIVE: We sought to review the risks and benefits of expectant management of severe preeclampsia remote from term, and to provide recommendations for expectant management, maternal and fetal evaluation, treatment, and indications for delivery.

METHODS: Studies were identified through a search of the MEDLINE database for relevant peer-reviewed articles published in the English language from January 1980 through December 2010. Additionally, the Cochrane Library, guidelines by organizations, and studies identified through review of the above documents and review articles were utilized to identify relevant articles. Where reliable data were not available, opinions of respected authorities were used.

RESULTS AND RECOMMENDATIONS: Published randomized trials and observational studies regarding management of severe preeclampsia occurring <34 weeks of gestation suggest that expectant management of selected patients can improve neonatal outcomes but that delivery is often required for worsening maternal or fetal condition. Patients who are not candidates for expectant management include women with eclampsia, pulmonary edema, disseminated intravascular coagulation, renal insufficiency, abruptio placentae, abnormal fetal testing, HELLP syndrome, or persistent symptoms of severe preeclampsia. For women with severe preeclampsia before the limit of viability, expectant management has been associated with frequent maternal morbidity with minimal or no benefits to the newborn. Expectant management of a select group of women with severe preeclampsia occurring <34 weeks' gestation may improve newborn outcomes but requires careful in-hospital maternal and fetal surveillance.

Key words: expectant management, fetal growth restriction, HELLP syndrome, severe preeclampsia

term complications for both the mother and her newborn.^{15,16} Maternal complications of severe preeclampsia (Table) (as well as myocardial infarction, stroke, acute respiratory distress syndrome, coagulopathy, severe renal failure, retinal injury) occur more commonly in the presence of preexistent medical disorders, and with acute maternal organ dysfunction related to preeclampsia.^{10,17} Maternal morbidities rarely persist after severe preeclampsia, although cardiovascular disease later in life is more common regardless of clinical presentation.^{15,16} Fetal and newborn complications of severe preeclampsia result from exposure to uteroplacental insufficiency and/or from preterm birth.^{1,10}

Historically, women with severe preeclampsia have had delivery initiated upon diagnosis in order to limit maternal complications from worsening disease.^{1,12} The

clinical course of severe preeclampsia is often characterized by progressive deterioration if delivery is not pursued.^{10,17} However, some have challenged the view that all patients with severe preeclampsia must be delivered expeditiously.⁷ The first attempts at expectant management were aimed at providing brief pregnancy prolongation to allow for antenatal corticosteroid administration, but the potential for longer expectant management was entertained because some patients remained stable or improved during initial observation. Further study has shown that median latency with expectant management ranges from 7-14 days.¹⁸

In this report, the risks and benefits of expectant management of severe preeclampsia remote from term are reviewed, and recommendations regarding expectant management, maternal and fetal evaluation, and indications

From the Society for Maternal-Fetal Medicine, Washington, DC (Publications Committee); and Division of Maternal Fetal Medicine, Department of Obstetrics and Gynecology, Clinical Perinatal Research, University of Cincinnati College of Medicine, Cincinnati, OH (Dr Sibai).

Received July 1, 2011; accepted July 7, 2011.

Reprints not available from the authors.

0002-9378/free

© 2011 Published by Mosby, Inc.

doi: 10.1016/j.ajog.2011.07.017

TABLE

Diagnostic criteria for preeclampsia, severe preeclampsia, and HELLP syndrome¹¹⁻¹⁴

- > Preeclampsia
 - Blood pressure ≥ 140 mm Hg or ≥ 90 mm Hg diastolic that occurs >20 wk' gestation in woman with previously normal blood pressure plus proteinuria defined as urinary excretion ≥ 0.3 g protein in 24-h urine specimen
 - > Severe preeclampsia (≥ 1 of following criteria is required)
 - Blood pressure ≥ 160 mm Hg systolic or ≥ 110 mm Hg diastolic on 2 occasions at least 6 h apart while patient is on bed rest
 - Proteinuria ≥ 5 g in 24-h urine specimen $\geq 3+$ on 2 random urine samples collected at least 4 h apart
 - Oliguria <500 mL in 24 h
 - Cerebral or visual symptoms
 - Pulmonary edema or cyanosis
 - Epigastric or right upper quadrant pain
 - Impaired liver function
 - Thrombocytopenia
 - Fetal growth restriction
 - > Superimposed preeclampsia (≥ 1 of following criteria is required)
 - New-onset proteinuria ≥ 0.3 g protein in woman with hypertension <20 wk' gestation
 - If hypertension and proteinuria present <20 wk' gestation
 - Sudden increase in proteinuria if both hypertension and proteinuria are present <20 wk' gestation
 - Sudden increase in hypertension in woman whose hypertension has previously been well controlled
 - Thrombocytopenia (platelet count $<100,000$ cells/mm³)
 - Increase in alanine aminotransferase or aspartate aminotransferase to abnormal levels
- Women with chronic hypertension who develop persistent headache, scotoma, or epigastric pain also may have superimposed preeclampsia
- > HELLP syndrome (differing diagnostic criteria have been reported, 2 commonly used criteria follow)
 - Sibai et al¹³ (each of following required)
 - (1) Hemolysis on peripheral smear, lactate dehydrogenase >600 U/L, or total bilirubin >1.2 mg/dL
 - (2) Aspartate aminotransferase >70 U/L
 - (3) Platelet count $<100,000$ cells/mm³
 - Martin et al¹⁴ (each of following required)
 - (1) Lactate dehydrogenase >600 U/L
 - (2) Aspartate aminotransferase or alanine aminotransferase >40 IU/L
 - (3) Platelet count $<150,000$ cells/mm³

SMFM. Severe preeclampsia. *Am J Obstet Gynecol* 2011.

for delivery are offered. For the purpose of this document, expectant management is defined as any attempt to delay delivery for antenatal corticosteroid administration or longer.

What are the benefits and risks of expectant management of severe preeclampsia <34 weeks' gestation?

Randomized trials

Only 2 randomized trials of delivery vs expectant management of preterm severe preeclampsia have been published.^{19,20}

Odendaal et al¹⁹ studied 38 women with severe preeclampsia between 28-34 weeks' gestation age and whose fetal weight was estimated to be between 650-

1500 g. Eighteen women received antenatal corticosteroids for fetal maturation and were then treated expectantly, with delivery only for specific maternal or fetal indications. Another 20 patients were assigned to receive antenatal corticosteroids with planned delivery after 48 hours. Latency to delivery (7.1 vs 1.3 days; $P < .05$) and gestational age at delivery (223 vs 221 days; $P < .05$) were both greater with expectant management while total neonatal complications were reduced (33% vs 75%; $P < .05$) compared with planned delivery.

Sibai et al²⁰ studied 95 women with severe preeclampsia and no concurrent

medical (eg, renal disease, insulin-dependent diabetes, connective tissue disease) or obstetric (eg, vaginal bleeding, premature rupture of membranes, multifetal gestation, preterm labor) complications at 28-32 weeks' gestation. Those randomized to expectant management delivered at a more advanced gestational age (32.9 vs 30.8 weeks; $P < .01$), and had newborns with higher birthweights (1622 vs 1233 g; $P < .01$) who required less frequent neonatal intensive care unit admission (76% vs 100%; $P < .01$). Newborns from the expectantly managed group had less frequent respiratory distress syndrome (22.4% vs 50%; $P = .002$) and necrotizing enterocolitis (0% vs 10.9%; $P = .02$), but were more frequently small for gestational age at birth (30.1 vs 10.9; $P = .04$). There were no cases of maternal eclampsia or pulmonary edema in either trial. Abruption placenta was similar in frequency between the randomized groups in both studies, but was more common in both the expectantly and nonexpectantly managed groups from the Odendaal et al¹⁹ trial (22% vs 15%) than in the Sibai et al²⁰ study (4.1% vs 4.3%). HELLP syndrome complicated only 2 expectantly managed cases and 1 aggressively managed case in the latter study (4.1% vs 2.1%).

Two additional randomized trials evaluated therapeutic interventions during expectant management. Fenakel et al²¹ described 49 women with severe preeclampsia at 26-36 weeks who were randomly assigned to receive either sublingual and oral nifedipine or intravenous and oral hydralazine treatments for severe hypertension during expectant management. Those assigned to nifedipine therapy delivered more frequently at ≥ 36 weeks, were less frequently diagnosed with acute fetal distress, and their infants had a shorter mean duration of neonatal intensive care unit stay than those assigned to hydralazine therapy ($P < .01$ for each). However, mean gestational age at delivery (34.6 vs 33.6 weeks; $P < .20$) and pregnancy prolongation (15.5 vs 9.5 days; $P < .07$) were not improved, and no differences in the frequencies of "major" or "minor" newborn complications were seen between groups. In multicenter

comparison of antihypertensive therapy alone vs antihypertensive therapy plus plasma volume expansion, Ganzevoort et al²² found that volume expansion gave no additional benefit among women expectantly managed with severe preeclampsia at 24–33 weeks 6 days.

Observational studies

Observational studies regarding expectant management of severe preeclampsia have varied in their inclusion criteria and indications for delivery.^{5,7,10,18,23–35} Some included only those women who remained stable after 24–48 hours of observation, while others included women expectantly managed from the time of diagnosis. A recent systematic review summarized the frequency of complications related to severe preeclampsia remote from term.¹⁸ Presented as (median; interquartile range [IQR]), complications of expectant management included: intensive care unit admission (median, 27.6%; IQR, 1.5–52.6), hypotension (median, 17.0%; IQR, 12.0–21.0), HELLP syndrome (median, 11.0%; IQR, 5.3–17.6), recurrent severe hypertension (median, 8.8%; IQR, 3.3–27.5), abruptio placentae (median, 5.1%; IQR, 2.2–8.5), pulmonary edema (median, 2.9%; IQR, 1.5–52.6), eclampsia (median, 1.1%; IQR, 0–2.0), subcapsular liver hematoma (median, 0.5%; IQR, 0.2–0.7), stroke (median, 0.4%; IQR, 0–3.1), stillbirth (median, 2.5%; IQR, 0–11.3), and neonatal death (median, 7.3%; IQR, 5.0–10.7). Small for gestational age infants were common (median, 36.8%; IQR, 20.5–53.8) after expectant management. Delivery for fetal (46%) or maternal (40%) indications was similarly frequent.

In summary, expectant management of severe preeclampsia occurring <34 weeks' gestation aimed at increasing gestational age at delivery and birth weight, and decreasing neonatal complications is appropriate in selected cases, but careful in-hospital maternal and fetal surveillance are recommended.

What is the initial evaluation and management of severe preeclampsia <34 completed weeks' gestation?

Women with suspected severe preeclampsia should be hospitalized to confirm the diagnosis, evaluate maternal

and fetal condition, and monitor for rapid progression of the disease. During this initial assessment, intravenous magnesium sulfate seizure prophylaxis has been suggested by some, and may be considered. Continuous fetal heart rate and uterine contraction monitoring are initiated if there is an intention to intervene for fetal benefit. Maternal assessment should include evaluation of vital signs and physical examination with specific attention for signs of preeclampsia and its complications. Laboratory tests should include at least a complete blood cell count with platelet count, serum creatinine, and liver enzymes (aspartate aminotransferase, alanine aminotransferase). Urinary protein or urinary total protein/creatinine ratio, to confirm the presence of significant proteinuria, are often evaluated from a random urine sample. However, because these tests do not reliably exclude significant proteinuria or accurately quantitate the amount of proteinuria, 24-hour urine collection and analysis should generally be performed. Coagulation studies including serum fibrinogen, prothrombin time, and partial thrombin time, and evaluation for hemolysis (peripheral smear, serum bilirubin and/or lactate dehydrogenase) should be considered if the platelet count is <100,000/mm³, if liver enzymes are elevated, or if there are findings suggestive of abruptio placentae. Ultrasound should be performed to evaluate for fetal presentation, evidence of growth restriction, and/or oligohydramnios.

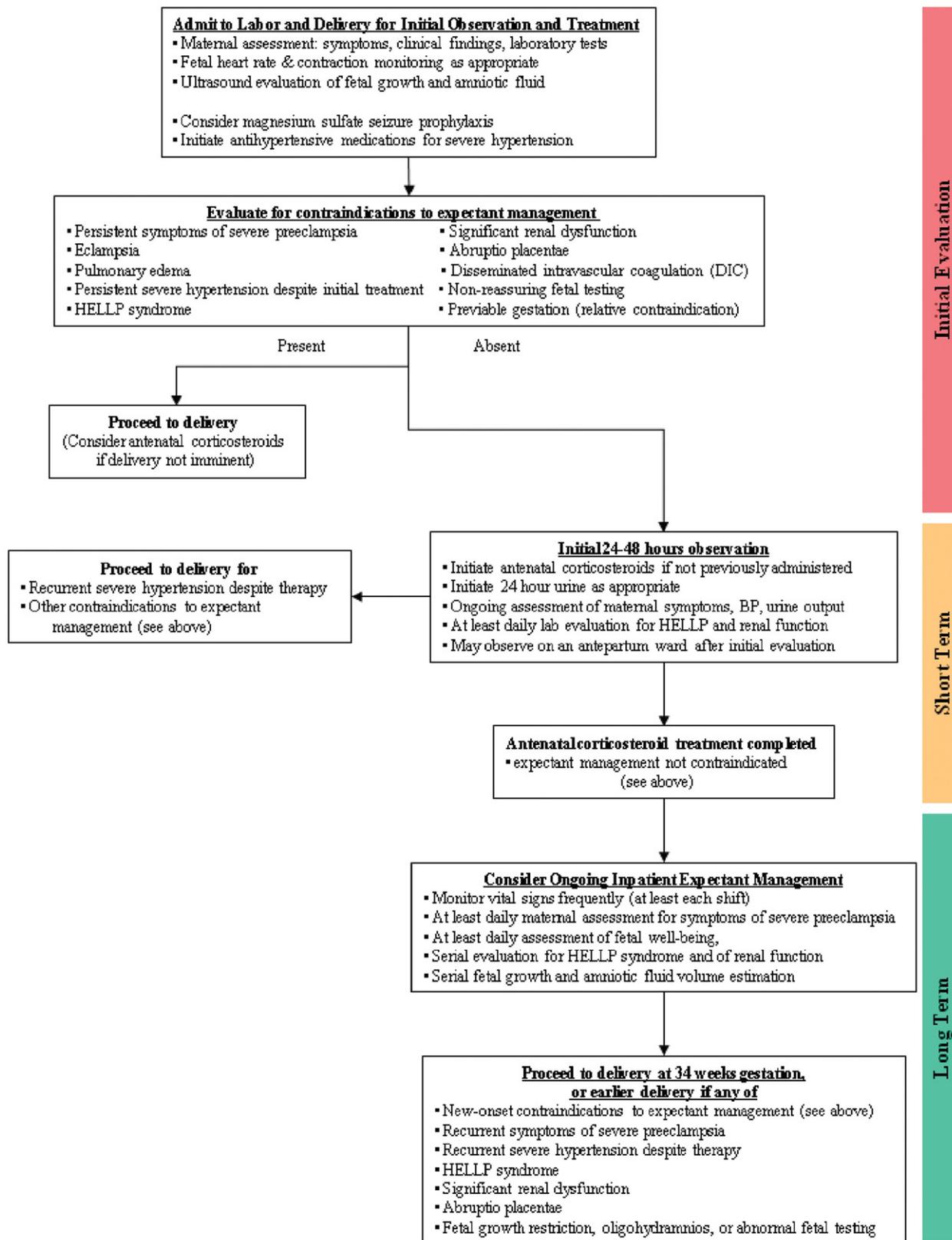
Women with persistent symptoms of severe preeclampsia, uncontrollable severe hypertension, eclampsia, pulmonary edema, abruptio placentae, disseminated intravascular coagulation, significant and new-onset renal dysfunction (serum creatinine \geq 1.5 mg/dL), HELLP syndrome, and those who have abnormal fetal surveillance results should typically be delivered (vaginal or cesarean delivery as appropriate) after initial maternal stabilization (Figure).¹⁰ The remainder may be candidates for short-term pregnancy prolongation to achieve the benefits of antenatal corticosteroid treatment, or for extended pregnancy prolongation to allow fetal growth and maturation. While data specific to expectantly managed severe

preeclampsia are limited, randomized controlled trials involving pregnancies complicated by hypertension syndromes have found antenatal corticosteroid treatment to result in less frequent respiratory distress syndrome (risk ratio [RR], 0.50; 95% confidence interval [CI], 0.35–0.72), neonatal death (RR, 0.50; 95% CI, 0.29–0.87), and intraventricular hemorrhage (RR, 0.38; 95% CI, 0.17–0.87).³⁶ In a single placebo-controlled study of weekly betamethasone for women with severe preeclampsia between 26–34 weeks' gestation, treatment (mean exposure 1.7 doses) reduced the frequencies of respiratory distress syndrome (RR, 0.53; 95% CI, 0.35–0.82) and intraventricular hemorrhage (RR, 0.35; 95% CI, 0.15–0.86), among other complications.³⁷ In this study, there were 2 maternal deaths among 218 pregnancies.

If not previously given, and if it is anticipated that there will be time for fetal benefit from this intervention, antenatal corticosteroid administration should be considered regardless of a plan for expectant management. Those who develop new-onset contraindications to expectant management before or after completion of antenatal corticosteroid treatment should be delivered (Figure). If the maternal and fetal conditions remain stable during initial inpatient monitoring, continued expectant management of women <34 weeks' gestational age is appropriate. Continuous fetal monitoring, and magnesium sulfate seizure prophylaxis if initiated, can be discontinued. Women with suspected fetal growth restriction and/or oligohydramnios are not typically considered to be candidates for expectant management beyond completion of antenatal corticosteroid therapy due to the increased risk of adverse outcomes including perinatal death.^{5,17,20,22,26} Management in these cases should be individualized and based on the severity of fetal growth restriction, the presence of coexisting oligohydramnios, and results of fetal surveillance. For the remaining women, the potential maternal risks and perinatal benefits of continued expectant management after antenatal corticosteroid treatment should be determined after consideration of clinical factors such as gestational age,

FIGURE

Clinical algorithm for management of suspected severe preeclampsia <34 weeks' gestation



BP, blood pressure.

SMFM. Severe preeclampsia. Am J Obstet Gynecol 2011.

maternal status, and likelihood of significant pregnancy prolongation.

Because of the potential for rapid deterioration of the maternal and/or fetal condition during expectant management of severe preeclampsia, such women are optimally cared for in a hospital with services capable of managing complicated obstetric cases and preterm newborns.¹⁰ Maternal evaluation should include monitoring of blood pressure, urine output, and signs or symptoms of concern (persistent headache, visual changes, epigastric pain, abdominal tenderness, or vaginal bleeding). The frequency and nature of fetal monitoring should be based on gestational age and fetal status. During initial expectant management, at least daily assessment of the complete blood cell count with platelet count, as well as liver and renal functions can help identify those in whom the disease is progressing and requires delivery. Evaluation of maternal coagulation parameters is not typically necessary. The frequency of subsequent laboratory testing can be determined based on the severity of illness and disease progression. Uric acid levels and changes in urinary protein concentrations do not reliably predict adverse maternal or perinatal outcomes and therefore serial measurement offers little clinical benefit.³⁸⁻⁴¹ Depending on the duration of expectant management, follow-up ultrasound examination for fetal growth evaluation and amniotic fluid volume estimation should also be performed. If contraindications to expectant management are not encountered by 34 weeks of gestation, delivery should be initiated at that time because of the ongoing risks to the mother and fetal risks during continued expectant management.

Should severe proteinuria alter the approach to management of severe preeclampsia?

The presence of severe proteinuria in women with severe preeclampsia undergoing expectant management is not associated with worse outcomes. In one study of 42 expectantly managed women with severe proteinuria (defined as ≥ 5 g/24 h), significant pregnancy prolongation occurred, maternal complications were not increased, and resolution of re-

nal dysfunction occurred in all women by 3 months after delivery.²³ A second study categorized women with severe preeclampsia according to the severity of proteinuria as mild (< 5 g/24 h), severe (5-9.9 g/24 h), or massive (> 10 g/24 h).⁴¹ No differences in the rates of eclampsia, abruptio placentae, pulmonary edema, HELLP syndrome, neonatal death, or neonatal morbidity were identified between these groups. Although the amount of proteinuria increases over time with expectant management, this change is not predictive of pregnancy prolongation or perinatal outcomes.³⁹ On the basis of these data, severe proteinuria alone and the degree of change in proteinuria should not be considered criteria to avoid or terminate expectant management.

Should expectant management be offered when HELLP syndrome is present?

Women with HELLP syndrome have been excluded from most published studies of expectantly managed preterm severe preeclampsia as these abnormalities are generally considered to be indications for delivery.^{10,19,20} Further, the diagnostic criteria used for HELLP syndrome have varied between publications.⁴² In a systematic review of 12 studies, Magee et al¹⁸ evaluated the frequency of complications that can occur when expectant management is undertaken in the setting of HELLP syndrome < 34 weeks' gestation. Median [IQR] latency to delivery was 5.8 days [0.8-10.3] and delivery for fetal indication was common (median, 70.8%; IQR, 53.9-89.0). Complications (median [interquartile range]) included recurrent severe hypertension (median, 46.2%; IQR, 33.6-58.8), abruptio placentae (median, 5.1%; IQR, 3.3-6.4), eclampsia (median, 0.8%; IQR, 0-4.9), subcapsular liver hematoma (median, 3.1%; IQR, 1.6-4.7), stroke (6.3%), stillbirth (median, 10.5%; IQR, 3.4-19.1), and neonatal death (median, 5.5%; IQR, 4.3-8.9). Delivery of a small for gestational age infant was common (56.3%). Maternal death has also occurred during expectant management of HELLP syndrome.⁴³

A recent metaanalysis of 11 trials evaluated the impact of antenatal maternal corticosteroid treatment on perinatal outcomes during expectant management of HELLP.⁴⁴ This systematic review found improved maternal platelet counts when corticosteroids are given, but there was no evidence of improvements in maternal mortality, severe maternal morbidities, or perinatal/infant deaths.

Given current evidence of brief latency and maternal risk without demonstrated fetal benefits, women with HELLP syndrome should not typically be managed expectantly, and vaginal or cesarean delivery should be pursued as appropriate. Antenatal corticosteroid administration may be given concurrently, if it is anticipated that there will be adequate time for fetal benefit from treatment, but the risk of surgical complications in the setting of thrombocytopenia should be considered. If delivery is delayed for antenatal corticosteroid administration (eg, for patients with incomplete findings of HELLP syndrome), magnesium sulfate seizure prophylaxis should be continued and continuous fetal monitoring should be performed because of the potential for eclampsia and fetal death. Delivery should be pursued if the maternal or fetal condition worsens, or upon completion of this treatment.^{5,10,20,21,27}

Should expectant management be offered when fetal growth restriction is suspected?

While no prospective trials have evaluated the benefits and risks of expectant management when fetal growth restriction is suspected in the setting of preterm severe preeclampsia, 2 retrospective observational studies have described outcomes for such pregnancies.^{22,26} In one study of volume expansion during expectant management of severe preeclampsia, those with suspected fetal growth restriction (defined as ultrasound estimated weight < 10 th percentile or abdominal circumference < 5 th percentile) had a median pregnancy prolongation of 7 days, and the frequency of adverse outcome (perinatal death, chronic lung disease, grade ≥ 3 intraventricular hemorrhage, or grade ≥ 2 periventricular leukomalacia) for this

group was similar to the overall cohort.²² A second study compared 14 women with severe preeclampsia and estimated fetal weight <10th percentile with 33 women without fetal growth restriction.²⁶ Only brief pregnancy prolongation (3.1 days) was seen with expectant management, and the incidences of abruption and neonatal morbidities were similar between those with or without fetal growth restriction. These investigators recommended delivery after antenatal corticosteroid administration in such cases. While published studies fail to demonstrate benefits from expectant management of severe preeclampsia with concurrent suspected fetal growth restriction, the number of subjects studied is small and there is a wide spectrum of severity of fetal growth restriction. The decision regarding expectant management of these patients should be individualized.

Should severe preeclampsia occurring before the limit of viability be treated expectantly?

Severe preeclampsia that develops near the limit of fetal viability is associated with a high likelihood of perinatal morbidities and mortality, regardless of expectant management.^{5,7,8,31,33,45-50} However, data regarding outcomes with expectant management categorized by gestational week at diagnosis are limited. Survival rates of 0/34 (0%), 4/22 (18.2%), and 15/26 (57.7%) have been reported after expectant management of severe preeclampsia initiated <23 weeks', at 23 weeks', and at 24 weeks' gestation, respectively.^{5,31,49,50} Other reports have also suggested rare survival with expectant management of severe preeclampsia <23-24 weeks' gestation.^{7,48} Explicit counseling regarding the likelihood of poor perinatal outcomes with expectant management should be provided. Delivery should be considered when severe preeclampsia occurs before the limit of viability (Figure).^{5,7,10,31,48-50}

What is the role of antihypertensive therapy during expectant management?

In women with severe preeclampsia, control of maternal blood pressure is necessary to decrease the risks of acute hypertension (eg, maternal cerebrovas-

cular accident, myocardial ischemia), but a dramatic decrease may also impair uteroplacental perfusion. Antihypertensive medications should be considered if systolic blood pressure remains persistently >160 mm Hg, or if diastolic blood pressure persists >110 mm Hg.¹⁰ Once treated, the target range should be a systolic blood pressure of 140-155 mm Hg and a diastolic blood pressure of 90-105 mm Hg.

Although parenteral antihypertensive therapy may be needed initially for acute control of blood pressure, oral medications can be utilized as expectant management is continued. Oral labetalol and calcium channel blockers have been commonly used.¹⁰ One approach is to begin an initial regimen of labetalol at 200 mg orally every 12 hours, and increase the dose up to 800 mg orally every 8-12 hours as needed (maximum total 2400 mg/d). If the maximum dose is inadequate to achieve the desired blood pressure goal, then short-acting oral nifedipine can be added at an initial dose of 10 mg orally every 6 hours and increased as needed up to 20 mg every 4 hours (40-120 mg/d). An alternative regimen is a long-acting preparation of nifedipine (up to 30-60 mg/d). Following initial control of severe hypertension, blood pressure should be measured at least every 6-8 hours. If there is recurrent persistent severe hypertension despite adequate oral or intravenous antihypertensive therapy, delivery should be pursued after maternal stabilization.

What strategies are available for fetal assessment during expectant management?

No randomized trials have identified an optimal method of fetal assessment during expectant management of severe preeclampsia, however there is agreement that fetal testing is indicated if the pregnancy is considered viable.^{5,19-33} Non-stress testing (NST) is recommended, but the optimal frequency of testing and the additional value of biophysical profile testing have not been determined. One approach for fetal surveillance involves at least daily NSTs, with biophysical profile testing performed should a non-reactive NST result be encountered. Follow-up fetal growth evaluation and

amniotic fluid volume estimation should also be performed. If fetal growth restriction is suspected, and expectant management is undertaken, then incorporation of Doppler blood flow studies into an individualized management scheme is appropriate.

What are the indications for delivery after expectant management?

In the published studies of preterm severe preeclampsia managed expectantly, delivery has typically been pursued at approximately 34 completed weeks' gestation. However, deterioration of maternal and/or fetal conditions prior to this gestational age is the most common reason for delivery.¹⁸ Maternal indications for delivery are delineated in Figure. Delivery should also be considered for women declining or noncompliant to ongoing inpatient observation; those developing persistent epigastric or right upper quadrant pain, nausea, or vomiting; and for those who develop preterm labor or premature rupture of membranes (Figure).^{5,11,12,19,20,26-33} When delivery is indicated, vaginal delivery can often be accomplished, but this is less likely with decreasing gestational age. With labor induction, the likelihood of cesarean delivery increases with decreasing gestational age in this setting (range, 93-97% <28 weeks', 53-65% at 28-32 weeks', and 31-38% at 32-34 weeks' gestation).⁵¹⁻⁵⁴

RECOMMENDATIONS

Levels I and II evidence, level A recommendation

1. Expectant management of severe preeclampsia remote from term is appropriate in selected cases, and is associated with pregnancy prolongation and improved newborn outcomes.

Levels II and III evidence, level B recommendation

2. Women with persistent symptoms of severe preeclampsia, uncontrollable severe hypertension, eclampsia, pulmonary edema, abruptio placentae, disseminated intravascular coagulation, significant and new-onset renal dysfunction, and those who have abnormal fetal surveillance results, should

Quality of evidence

The quality of evidence for each included article was evaluated according to the categories outlined by the US Preventative Services Task Force:

- I** Properly powered and conducted randomized controlled trial; well-conducted systematic review or metaanalysis of homogeneous randomized controlled trials.

- II-1** Well-designed controlled trial without randomization.

- II-2** Well-designed cohort or case-control analytic study.

- II-3** Multiple time series with or without the intervention; dramatic results from uncontrolled experiments.

- III** Opinions of respected authorities, based on clinical experience; descriptive studies or case reports; reports of expert committees.

Recommendations are graded in the following categories:

Level A

The recommendation is based on good and consistent scientific evidence.

Level B

The recommendation is based on limited or inconsistent scientific evidence.

Level C

The recommendation is based on expert opinion or consensus.

typically be delivered after initial maternal stabilization.

Level I evidence,

level A recommendation

3. If not previously given, and if it is anticipated that there will be time for fetal benefit from this intervention before delivery, antenatal corticosteroid administration should be considered regardless of a plan for expectant management.

Level III evidence,

level C recommendation

4. Because of the ongoing risks to the mother and fetal risks during continued expectant management, delivery for severe preeclampsia should be undertaken at 34 weeks' gestation for those who remain pregnant to this gestational age.

Level II evidence,

level A recommendation

5. Severe proteinuria alone and the degree of change in proteinuria should not be considered criteria to avoid or terminate expectant management.

Levels I and II evidence,

level A recommendation

6. Women with HELLP syndrome should not typically be managed expectantly. Vaginal or cesarean delivery should be pursued as appropriate.

Level II and III evidence,

level B recommendation

7. The decision regarding expectant management of severe preeclampsia with concurrent suspected fetal growth restriction should be individualized.

Levels I and II evidence,

level B recommendation

8. Explicit counseling regarding the potential maternal risks should be provided and delivery should be considered when severe preeclampsia occurs before the limit of viability. ■

This opinion was developed by the Publications Committee of the Society for Maternal-Fetal Medicine with the assistance of Baha M. Sibai, MD, and was approved by the executive committee of the society on June 30, 2011. Dr Sibai and each member of the publications committee (Brian Mercer, MD [Chair], Vincenzo Berghella, MD, Sean Blackwell, MD, Joshua Copel, MD, William Grobman, MD, MBA, Cynthia Gyamfi, MD, Donna Johnson, MD, Sarah Kilpatrick, MD, PhD, George Macones, MD, George Saade, MD, Hyagriv Simhan, MD, Lynn Simpson, MD, Joanne Stone, MD, Michael Varner, MD, Ms Deborah Gardner) have submitted a conflict of interest disclosure delineating personal, professional, and/or business interests that might be perceived as a real or potential conflict of interest in relation to this publication.

REFERENCES

1. Sibai B, Dekker G, Kupfermich M. Preeclampsia. *Lancet* 2005;365:785-99. Level III.
2. Kuklina EV, Aya C, Callaghan WM. Hypertensive disorders and severe obstetric morbidity in the United States. *Obstet Gynecol* 2009;113:1299-306. Level II-3.
3. Catov JM, Ness RB, Kip KE, Olsen J. Risk of early or severe preeclampsia related to preexisting conditions. *Int J Epidemiol* 2007;36:412-9. Level II-3.
4. Zhang J, Meikle S, Trumble A. Severe maternal morbidity associated with hypertensive dis-

orders in pregnancy in the United States. *Hypertens Pregnancy* 2003;22:203-12. Level II-3.

5. Haddad B, Deis S, Goffinet F, Daniel BJ, Cabrol D, Sibai BM. Maternal and perinatal outcomes during expectant management of 239 severe preeclamptic women between 24 and 33 weeks' gestation. *Am J Obstet Gynecol* 2004;190:1590-5. Level II-2.

6. Gupta LM, Gaston L, Chauhan SP. Detection of fetal growth restriction with preterm severe preeclampsia: experience at two tertiary centers. *Am J Perinatol* 2008;25:247-9. Level II-3.

7. Sibai BM, Akl S, Fairlie F, Moretti M. A protocol for managing severe preeclampsia in the second trimester. *Am J Obstet Gynecol* 1990;163:733-8. Level II-2.

8. Visser W, Wallenburg HCS. Maternal and perinatal outcome of temporizing management in 254 consecutive patients with severe preeclampsia remote from term. *Eur J Obstet Gynecol Reprod Biol* 1995;63:147-54. Level II-2.

9. Vigil-DeGarcia P, Montufar-Rueda C, Ruiz J. Expectant management of severe preeclampsia between 24 and 34 weeks' gestation. *Eur J Obstet Gynecol Reprod Biol* 2003;107:24-7. Level II-2.

10. Sibai BM, Barton JR. Expectant management of severe preeclampsia remote from term: patient selection, treatment, and delivery indications. *Am J Obstet Gynecol* 2007;196:514e1-9. Level II-2.

11. Report of the National High Blood Pressure Education Program. Working group report on high blood pressure in pregnancy. *Am J Obstet Gynecol* 2000;183:S1-22. Level III.

12. American College of Obstetricians and Gynecologists. Diagnosis and management of preeclampsia and eclampsia: ACOG practice bulletin no. 33. *Obstet Gynecol* 2002;99:159-67. Level III.

13. Sibai BM, Ramadan MK, Usta I, Salama M, Mercer BM, Friedman SA. Maternal morbidity and mortality in 442 pregnancies with hemolysis, elevated liver enzymes, and low platelets (HELLP syndrome). *Am J Obstet Gynecol* 1993;169:1000-6. Level III.

14. Martin JN Jr, Blake PG, Perry KG, McCaul JF, Hess LW, Martin RW. The natural history of HELLP syndrome: patterns of disease progression and regression. *Am J Obstet Gynecol* 1991;164:1500-9. Level III.

15. Magnussen EB, Vatlen LJ, Lund-Nilsen TI, et al. Pregnancy cardiovascular risk factors as predictors of preeclampsia: population based cohort study. *BMJ* 2007;335:978-81. Level II-2.

16. Lykke A, Langoff-Ross J, Sibai BM, et al. Hypertensive pregnancy disorders and subsequent cardiovascular morbidity and type 2 diabetes mellitus in the mother. *Hypertension* 2009;53:944-51. Level II-2.

17. Schiff E, Friedman SA, Sibai BM. Conservative management of severe preeclampsia remote from term. *Obstet Gynecol* 1994;84:626-30. Level III.

- 18.** Magee LA, Yong PJ, Espinosa V, Côté AM, Chen I, von Dadelszen P. Expectant management of severe preeclampsia remote from term: a structured systematic review. *Hypertens Pregnancy* 2009;28:312-47. Level I.
- 19.** Odendaal HJ, Pattinson RC, Bam R, Grove D, Kotze TJ. Aggressive or expectant management for patients with severe preeclampsia between 28-34 weeks' gestation: a randomized controlled trial. *Obstet Gynecol* 1990;76:1070-5. Level I.
- 20.** Sibai BM, Mercer BM, Schiff E, Friedman SA. Aggressive versus expectant management of severe preeclampsia at 28 to 32 weeks' gestation: a randomized controlled trial. *Am J Obstet Gynecol* 1994;171:818-22. Level I.
- 21.** Fenakel K, Kenakel G, Appleman Z, et al. Nifedipine in treatment of severe preeclampsia. *Obstet Gynecol* 1991;77:331-7. Level I.
- 22.** Ganzevoort W, Rep A, Bousel GJ, et al. A randomized controlled trial comparing two temporizing management strategies, one with and one without plasma volume expansion, for severe preeclampsia. *BJOG* 2005;112:1358-68. Level I.
- 23.** Chua S, Redman CW. Prognosis for preeclampsia complicated by 5 g or more of proteinuria in 24 hours. *Eur J Obstet Gynecol Reprod Biol* 1992;43:9-12. Level II-3.
- 24.** Olah KS, Redman WG, Gee H. Management of severe, early pre-eclampsia: is conservative management justified? *Eur J Obstet Gynecol Reprod Biol* 1993;51:175-80. Level II-2.
- 25.** van Pampus MG, Wolf H, Westenberg SM, der Post V, Bonsel GJ, Treffers PE. Maternal and perinatal outcome after expectant management of HELLP syndrome compared with preeclampsia without HELLP syndrome. *Eur J Obstet Gynecol Reprod Biol* 1998;76:31-6. Level II-2.
- 26.** Chammas MF, Nguyen TM, Li MA, Nuwayhid BS, Castro LC. Expectant management of severe preterm preeclampsia: is intrauterine growth restriction an indication for immediate delivery? *Am J Obstet Gynecol* 2000;183:853-8. Level II-3.
- 27.** Hall DR, Odendaal HJ, Steyn DW, Grove D. Expectant management of early onset, severe preeclampsia; maternal outcome. *Br J Obstet Gynaecol* 2000;107:1252-7. Level II-3.
- 28.** Hall DR, Odendaal HJ, Kristen GF, Smith J, Grove D. Expectant management of early onset, severe preeclampsia: perinatal outcome. *Br J Obstet Gynaecol* 2000;107:1258-64. Level II-3.
- 29.** Shear RM, Rinfret D, Leduc L. Should we offer expectant management in cases of severe preterm preeclampsia with fetal growth restriction? *Am J Obstet Gynecol* 2005;192:1119-25. Level II-3.
- 30.** Oettle C, Hall D, Roux A, Grove D. Early onset severe preeclampsia: expectant management at a secondary hospital in close association with a tertiary institution. *BJOG* 2005;112:84-8. Level II-3.
- 31.** Bombrys AE, Barton JR, Nowacki E, Habli M, Sibai BM. Expectant management of severe preeclampsia at <27 weeks' gestation: maternal and perinatal outcomes according to gestational age by weeks at onset of expectant management. *Am J Obstet Gynecol* 2008;199:247.e1-6. Level II-2.
- 32.** Bombrys AE, Barton JR, Habli M, Sibai BM. Expectant management of severe preeclampsia at 27^{0/7}-33^{6/7} weeks' gestation: maternal and perinatal outcomes according to gestational age by weeks at onset of expectant management. *Am J Perinatol* 2009;26:441-6. Level II-3.
- 33.** Hall DR, Grove D, Carstens E. Early-preeclampsia: what proportion of women qualify for expectant management and if not, why not? *Eur J Obstet Gynecol Reprod Biol* 2006;128:169-74. Level II-3.
- 34.** Sarsam DS, Shamden M, Al Wazan R. Expectant versus aggressive management in severe preeclampsia remote from term. *Singapore Med J* 2008;49:698-703. Level II-1.
- 35.** Abdel-Hady el-S, Fawzy M, El-Negeri M, Nezar M, Ragab A, Helal AS. Is expectant management of early-onset severe preeclampsia worthwhile in low-resource settings? *Arch Gynecol Obstet* 2010;282:23-7. Level II-2.
- 36.** Roberts D, Dalziel SR. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. *Cochrane Database Syst Rev* 2006;3:CD004454. Level I.
- 37.** Amorim MM, Santos LC, Faundes A. Corticosteroid therapy for prevention of respiratory distress syndrome in severe preeclampsia. *Am J Obstet Gynecol* 1999;180:1283-8. Level I.
- 38.** Thangaratnam S, Ismail KMK, Sharp S, et al. Accuracy of serum uric acid in predicting complications of pre-eclampsia: a systematic review. *BJOG* 2006;113:369-78. Level I.
- 39.** Schiff E, Friedman SA, Kao L, Sibai BM. The importance of urinary protein excretion during conservative management of severe preeclampsia. *Am J Obstet Gynecol* 1996;175:1313-6. Level II-3.
- 40.** Hall DR, Odendaal HJ, Stein DW, Grive D. Urinary protein excretion and expectant management of early onset, severe preeclampsia. *Int J Gynaecol Obstet* 2002;77:1-6. Level II-3.
- 41.** Newman MG, Robichaux AG, Stedman CM, et al. Perinatal outcomes in preeclampsia that is complicated by massive proteinuria. *Am J Obstet Gynecol* 2003;188:264-8. Level II-3.
- 42.** Sibai BM. Diagnosis, controversies, and management of the syndrome of hemolysis, elevated liver enzymes, and low platelet count. *Obstet Gynecol* 2004;103:981-91. Level II-2.
- 43.** van Runnard Heimel PJ, Huisjes AJM, Fraux A, Koopman C, Bots ML, Bruinse HW. A randomized placebo-controlled trial of prolonged prednisolone administration to patients with HELLP syndrome remote from term. *Eur J Obstet Gynecol Reprod Biol* 2006;128:187-93. Level I.
- 44.** Woudstra DM, Chandra S, Hofmeyr GJ, Dowswell T. Corticosteroids for HELLP (hemolysis, elevated liver enzymes, low platelets) syndrome in pregnancy. *Cochrane Database Syst Rev* 2010;9:CD008148. Level I.
- 45.** Moodley J, Koranteng SA, Rout C. Expectant management of early onset of severe preeclampsia in Durban. *S Afr Med J* 1993;83:584-7. Level II-3.
- 46.** Hall DR, Odendaal HJ, Steyn DW. Expectant management of severe pre-eclampsia in the mid-trimester. *Eur J Obstet Gynecol* 2001;96:168-72. Level II-3.
- 47.** Jenkins SM, Head BB, Hauth JC. Severe preeclampsia at <25 weeks of gestation: maternal and neonatal outcomes. *Am J Obstet Gynecol* 2002;186:790-5. Level II-3.
- 48.** Gaugler-Senden IPM, Huijssoon AG, Visser W, Steegers EAP, deGroot CJM. Maternal and perinatal outcome of preeclampsia with onset before 24 weeks' gestation: audit in a tertiary referral center. *Eur J Obstet Gynecol Reprod Biol* 2006;128:216-21. Level II-3.
- 49.** Budden A, Wilkinson L, Buksh MJ, McCowan L. Pregnancy outcome in women presenting with pre-eclampsia at less than 25 weeks' gestation. *Aust N Z J Obstet Gynaecol* 2006;46:407-12. Level II-3.
- 50.** Sezik M, Ozkaya O, Sezik HT, Yapar EG. Expectant management of severe preeclampsia presenting before 25 weeks of gestation. *Med Sci Monit* 2007;13:523-7. Level II-3.
- 51.** Nassar AH, Adra AA, Chakhtoura N, Beydoun S. Severe preeclampsia remote from term: labor induction or elective cesarean delivery? *Am J Obstet Gynecol* 1998;179:1210-3. Level III.
- 52.** Alexander JM, Bloom SL, McIntire DD, Levono KJ. Severe preeclampsia and the very-low birth weight infant: is induction of labor harmful? *Obstet Gynecol* 1999;93:485-8. Level III.
- 53.** Blackwell SC, Redman ME, Tomlinson M, et al. Labor induction for the preterm severe pre-eclamptic patient: is it worth the effort? *J Matern Fetal Med* 2001;10:305-11. Level III.
- 54.** Alanis MC, Robinson CJ, Hulsey TC, Ebeling M, Johnson DJ. Early-onset severe preeclampsia: induction of labor vs elective cesarean delivery and neonatal outcomes. *Am J Obstet Gynecol* 2008;199:262.e1-6. Level II-3.

The practice of medicine continues to evolve, and individual circumstances will vary. This opinion reflects information available at the time of its submission for publication and is neither designed nor intended to establish an exclusive standard of perinatal care. This publication is not expected to reflect the opinions of all members of the Society for Maternal-Fetal Medicine.