Preeclampsia & Eclampsia

See also HTN in pregnancy

Background

1. Definition[1]
    - Preeclampsia: HTN with proteinuria occurring after 20 wks gestation
        - SBP ≥ 140 and DBP ≥ 90 on at least 2 occasions >6 hours apart
        - Proteinuria
            - > 0.3 g/24 hr urine collection
            - ≥1+ urine protein on dipstick x2 at least 6 hrs apart & random urine protein/creatinine ratio > 0.21 suggestive of significant proteinuria; needs confirmation with 24 hour urine
    - Severe preeclampsia
        - SBP ≥ 160 or DBP ≥ 110 on at least 2 occasions no less than 6 hrs apart
        - Marked proteinuria (>5 g/24 hr) or ≥ 3+ protein on 2 random urine specimens collected at least 4 hrs apart
        - Signs & symptoms of end organ damage
            - Oliguria < 500 mL/ 24 hrs
            - Cerebral or visual disturbances
            - Pulmonary edema or cyanosis
            - Epigastric or RUQ pain
            - Abnormal liver function
            - Thrombocytopenia < 100,000/mm3
            - Fetal growth restriction
    - HELLP syndrome
        - Variant of severe preeclampsia
        - Hemolysis, Elevated LFTs, Low Platelets
    - Eclampsia
        - Preeclampsia with seizures or coma
        - Seizures are generalized tonic-clonic

Pathophysiology

1. Pathology of disease
    - Unknown
2. Incidence, prevalence
    - 6% of pregnant women (2-12%)
3. Risk factors
    - Preeclampsia in previous pregnancy (especially if severe or before 32 wks gestation) or in family history
    - Chronic hypertension, chronic renal disease, pregestational diabetes mellitus
    - Elevated body mass index
    - Nulliparity
    - Multiple gestation
    - Antiphospholipid antibody syndrome
    - Maternal age > 40 yrs
    - Twin gestation

4. Morbidity/mortality
    - Can be associated with significant maternal and fetal complications as well as death (accounts for 12% perinatal mortality worldwide)
    - Maternal
        - HELLP, eclampsia
        - DIC
        - Pulmonary edema
        - Acute renal failure
        - Stroke
        - Encephalopathy
        - Heart failure
        - Hepatocellular damage or hepatic rupture
    - Fetal
        - Preterm birth with associated complications
        - Small for gestational age

Diagnostics

1. History
    - May have symptoms of end organ damage especially with severe preeclampsia such as headache or visual disturbances, shortness of breath, epigastric or RUQ pain, increased edema particularly of hands and face
    - HELLP may present with flu-like symptoms, nausea, vomiting, RUQ or epigastric pain
2. Physical exam
    - See also Definition
    - Preeclampsia
        - SBP $\geq$ 140 and DBP $\geq$ 90 on at least 2 occasions no less than 6 hours apart
    - Severe preeclampsia
        - SBP $\geq$ 160 or DBP $\geq$ 110 on at least 2 occasions no less than 6 hrs apart
        - Pulmonary edema, RUQ/epigastric tenderness, increased edema (particularly hands/face), hyperreflexia may be noted on exam
    - HELLP
        - BPs may be WNL
        - RUQ/epigastric tenderness may be noted
    - Eclampsia
        - Seizure activity/postictal state
3. Diagnostic testing (Diagnostic Criteria noted in the Definitions)
    - See also Definition
    - Labs: CBC, electrolytes, U/A, uric acid, BUN/Cr, LFTs, consider T&C if worried about abruption/DIC
        - Platelets < 100,000
        - Hgb may be increased due to hemoconcentration or decreased due to hemolysis
        - Elevated transaminases suggestive of HELLP
        - BUN/creatinine increase usually associated with later stage

- Consider LDH, peripheral smear & coagulation profile if suspect severe disease
    - LDH > 600/L suggestive of hemolysis/liver dysfunction

Differential Diagnosis

1. Chronic hypertension
2. Chronic renal disease
3. Immune or thrombotic thrombocytopenic purpura
4. Gallbladder disease
5. Pancreatitis
6. Antiphospholipid syndrome
7. Hemolytic Uremic syndrome
8. Seizure disorder
9. Acute fatty liver of pregnancy
10. Severe gestational hypertension (no proteinuria)

Therapeutics

1. Mild preeclampsia
    - Antepartum surveillance (outpatient management is option if good follow-up can be ensured) (SOR:B)[2,4]
        - Measure BP twice weekly
        - Labs (CBC, platelets, ALT, AST, LDH, uric acid, creatinine) weekly
        - Proteinuria evaluations (urine dipstick or random protein/ creatinine ratios at each visit; periodic 24 hr urine collections)
        - NST 2x weekly
        - AFI 1-2x weekly
        - BPP weekly (can replace AFI or one of NSTs)
        - US for fetal growth every 3-4 wks to r/o IUGR (can also assess umbilical artery systolic/diastolic ratios as an early indicator of uteroplacental insufficiency)
    - Delivery
        - $\geq$34 wks with labor, ROM, abnormal fetal testing, IUGR
        - $\geq$37 wks & Bishop score $\geq$6
        - No later than 40 wks to deliver
2. Severe preeclampsia
    - Inpatient management only
    - Sample admission orders
        - Bedrest with seizure precautions
        - VS, deep tendon reflexes, mental status check every 15-60 minutes until stable, then every hour while on magnesium sulfate
        - I&Os (Foley catheter often needed)
        - IVFs (LR) 75 mL/hr IV to maintain urine output of 30 mL/hr; total intake not > than 125 mL/hr
        - Urinalysis (protein)
        - CBC with platelets, peripheral smear
        - CMP, LDH, uric acid
        - 24 hr urine collection for protein
        - Continuous electronic fetal heart rate monitoring

        - US for fetal weight, BPP, umbilical artery Dopplers
        - OB/MFM consult
        - Medications
            - Magnesium sulfate (see below)
            - Antihypertensives (see below)
            - Corticosteroids (if EGA is between 24 and 34 wks)
                - Betamethasone 12 mg IM, then repeat dose in 24 hrs OR
                - Dexamethasone 6 mg IM then every 12 hrs x 4 total
            - Calcium gluconate 1 g at bedside
    - Delivery
        - Vaginal delivery preferred unless EGA < 30 wks or Bishop score < 6, then consider C/S
        - Start Magnesium sulfate and deliver if maternal decompensation (eg. HELLP, signs of impending eclampsia, pulmonary edema), non-reassuring fetal testing, labor, ROM, ≥34 wks EGA
        - < 23 wks EGA, consider termination
        - 23-32 wks
            - Corticosteroids (24-34 wks EGA)
            - Antihypertensives if needed
            - Daily evaluation of maternal/fetal status
            - Deliver at 34 wks unless earlier maternal/fetal decompensation (SOR:B)[2,3]
        - 33-34 wks
            - Corticosteroids (wait 24 -48 hrs for full administration, then deliver)
            - Magnesium sulfate
3. Eclampsia
    - Delivery is mandatory, even if fetus is premature, however need to stabilize by controlling seizure first
    - Vaginal delivery preferred
    - High dose MgSO4 to treat seizures (see preeclampsia treatment)
        - If already on MgSO4 another bolus of 2g IV over 15-20 min is advised BEFORE using other agents if no signs of MgSO4 toxicity
    - Benzodiazepines, phenytoin, & barbiturates (ie phenobarbital) prn
        - All may lead to neonatal apnea
    - Hydralazine or labetalol to treat HTN (see below)
4. Antihypertensives if SBP > 160 or DBP > 105-110 mmHg:
    - Goal is to achieve systolic 140-155 & diastolic 90-105
    - Hydralazine 5-10 mg IV every 15-20 min to max of 30 mg
    - Labetalol 20 mg IV, then 40 mg IV if not effective within 10 min, then 80 mg q 10 min to max of 220 mg in 24 hr
    - Nitroprusside
        - Last resort due to potential fetal cyanide poisoning if used > 4 hrs
5. Magnesium sulfate (MgSO4) to control or prevent seizures (SOR:A)[1,2]
    - Loading dose 4-6 g in 100 mL fluid IV over 15-20 min
    - Maintenance drip 2 g/hr IV

- Hold maintenance dose and check stat magnesium level if:
  - Patellar reflex disappears
    - If no perceptible reflex even prior to starting MgSO4, can check serum magnesium levels every 4-6hrs; therapeutic level is 5-7
  - Depressed respiration
  - Urine output < 30 mL/hr
- May give MgSO4 IM (onset slower than IV and more painful)
  - 10 g deep IM loading dose (5 g IM each buttock)
  - 5 g deep IM q4hr (maintenance)
- Toxicity dose dependent, antidote: Ca gluconate 1 g IV over 5-10 min

Prognosis

1. Perinatal mortality for preeclampsia has declined but can still be fatal
2. 29-30% risk of recurrence of mild preeclampsia (2% risk of severe preeclampsia with prior mild preeclampsia; 7.5% risk if prior severe preeclampsia); more frequent if preeclampsia occurred earlier in pregnancy
3. Preeclampsia may be predictive of subsequent vascular disease[6]

Prevention

1. Bed rest
   - No evidence in support
2. Possible prophylaxis in high-risk pts
   - Calcium if high risk or low dietary calcium intake (SOR:A)[5]
   - Aspirin
     - Reduces risk of developing preeclampsia
       - 17% reduction for women at increased risk
       - 25% reduction for women at high risk

References

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5. Atallah AN, Hofmeyr GJ, Duley L. Calcium supplementation during pregnancy for preventing hypertensive disorders and related problems. Cochrane Databse Syst Rev 2002;1.
6. Bellamy L, Casas J, Hingorani A, Williams DJ. Pre-eclampsia and risk of cardiovascular disease and cancer in later life: systematic review and meta-analysis. BMJ 2007;335 (online Nov 2007)

Evidence-Based Inquiry

1. Should we prescribe bed rest for hypertensive disorders of pregnancy?
2. Does bed rest for preeclampsia improve neonatal outcomes?

3. Is aspirin safe and effective for the primary prevention of preeclampsia?
4. Does low-dose aspirin therapy prevent preeclampsia in pregnant women at increased risk?
5. Does low-dose aspirin reduce preeclampsia and other maternal-fetal complications?

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